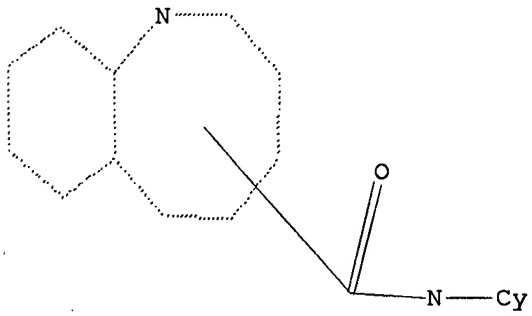
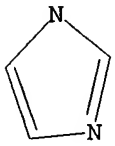
```
=> d his

     (FILE 'HOME' ENTERED AT 11:07:30 ON 12 JUN 2007)

     FILE 'REGISTRY' ENTERED AT 11:08:06 ON 12 JUN 2007
L1             STRUCTURE UPLOADED
L2               0 S L1
L3              54 S L1 SSS FUL
L4              54 S L3 AND CAPLUS/LC

     FILE 'CAPLUS' ENTERED AT 11:11:58 ON 12 JUN 2007
L5              16 S L4

=> d l1
L1 HAS NO ANSWERS
L1                STR
```





Structure attributes must be viewed using STN Express query preparation.

```
=> d ibib abs hitstr total
```

L5 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:148015 CAPLUS
DOCUMENT NUMBER: 146:308460
TITLE: Isolation and characterization of human immunodeficiency virus type 1 resistant to the small-molecule CCR5 antagonist TAK-652
AUTHOR(S): Baba, Masanori; Miyake, Hiroshi; Wang, Xin; Okamoto, Mika; Takashima, Katsunori
CORPORATE SOURCE: Division of Antiviral Chemotherapy, Center for Chronic Viral Diseases, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, 890-8544, Japan
SOURCE: Antimicrobial Agents and Chemotherapy (2007), 51(2), 707-715
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB TAK-652, a novel small-mol. chemokine receptor antagonist, is a highly potent and selective inhibitor of CCR5-using (R5) human immunodeficiency virus type 1 (HIV-1) replication in vitro. Since TAK-652 is orally bioavailable and has favorable pharmacokinetic profiles in humans, it is considered a promising candidate for an entry inhibitor of HIV-1. To investigate the resistance to TAK-652, peripheral blood mononuclear cells were infected with the R5 HIV-1 primary isolate KK and passaged in the presence of escalating concns. of the compound for more than 1 yr. After 67 wk of cultivation, the escape virus emerged even in the presence of a high concentration of TAK-652. This virus displayed more than 200,000-fold resistance to TAK-652 compared with the wild type. The escape virus appeared to have cross-resistance to the structurally related compound TAK-779 but retained full susceptibility to TAK-220, which is from a different class of CCR5 antagonists. Furthermore, the escape virus was unable to use CXCR4 as a coreceptor. Anal. for Env amino acid sequences of escape viruses at certain points of passage revealed that amino acid changes accumulated with an increasing number of passages. Several amino acid changes not only in the V3 region but also in other Env regions seemed to be required for R5 HIV-1 to acquire complete resistance to TAK-652.

IT 497223-28-6, TAK-652
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human immunodeficiency virus type 1 resistant to the small-mol. CCR5 antagonist TAK-652)

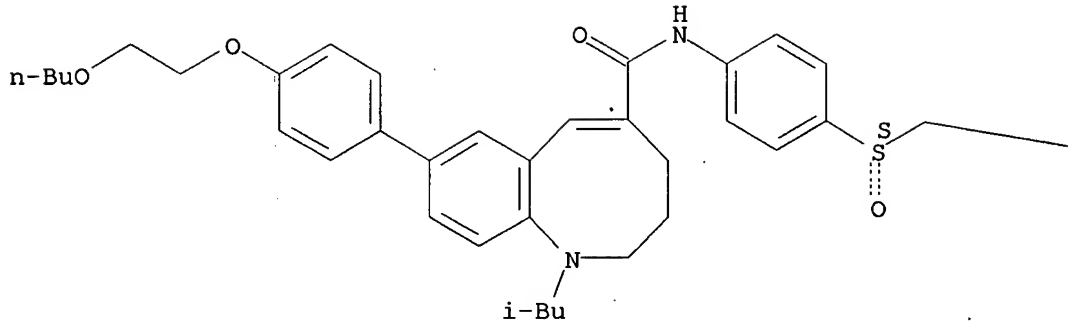
RN 497223-28-6 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

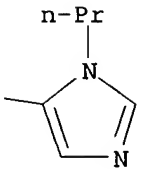
CRN 497223-25-3
CMF C41 H52 N4 O4 S

Absolute stereochemistry. Rotation (-).

PAGE 1-A

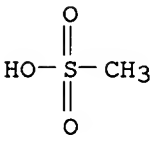


PAGE 1-B



CM 2

CRN 75-75-2
CMF C H4 O3 S



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:119657 CAPLUS
DOCUMENT NUMBER: 146:182972
TITLE: Methods for reducing viral load in HIV-1-infected patients
INVENTOR(S): Olson, William C.; Maddon, Paul J.; Pevear, Daniel C.; Israel, Robert J.; Murga, Jose D.
PATENT ASSIGNEE(S): Progenics Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 97pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007014114	A2	20070201	WO 2006-US28565	20060721
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2007026441	A1	20070201	US 2006-491330	20060721
PRIORITY APPLN. INFO.:			US 2005-702064P	P 20050722
			US 2005-701889P	P 20050723
			US 2005-711528P	P 20050826
			US 2005-715619P	P 20050909

AB The authors disclose a method for reducing viral load in an HIV-1-infected human subject. The method comprises the administration at a predefined intervals of (a) a humanized antibody designated PRO 140, or of (b) an anti-CCR5 receptor monoclonal antibody. The authors also disclose a treatment comprising the administration of (a) a monoclonal antibody which (i) binds to a CCR5 receptor on the surface of the subject's CD4+ cells and (ii) inhibits fusion of HIV-1 to CCR5+CD4+ cells, and (b) a non-antibody CCR5 receptor antagonist, in therapeutic amts.

IT 497223-28-6, TAK-652
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(with anti-CCR5 antibody for combination therapy in human immunodeficiency virus infection)

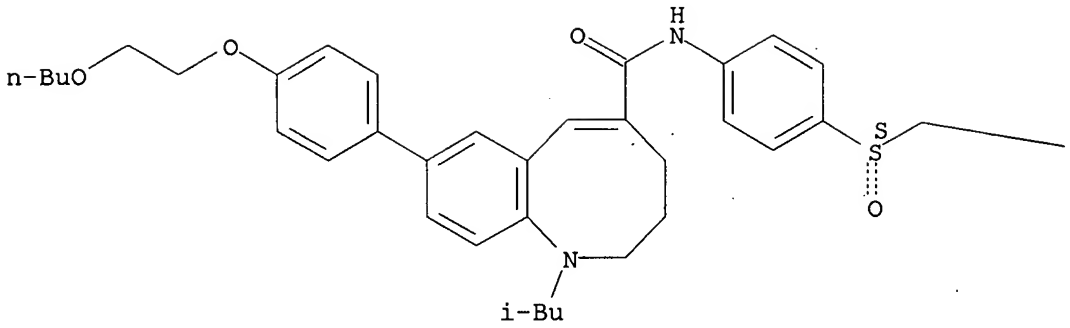
RN 497223-28-6 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

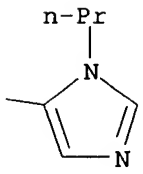
CRN 497223-25-3
CMF C41 H52 N4 O4 S

Absolute stereochemistry. Rotation (-).

PAGE 1-A

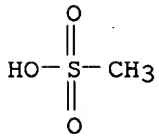


PAGE 1-B



CM 2

CRN 75-75-2
CMF C H4 O3 S

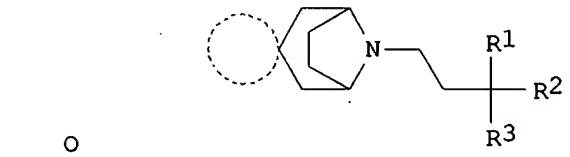


L5 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:578211 CAPLUS
DOCUMENT NUMBER: 145:62897
TITLE: Preparation of spirotropane compounds and therapeutic use as modulators of chemokine receptor activity
INVENTOR(S): Chan Chun Kong, Laval; Moinet, Christophe; Courchesne, Marc; Vaillancourt, Louis; Blais, Charles; Bubenik, Monica
PATENT ASSIGNEE(S): Virochem Pharma Inc., Can.
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

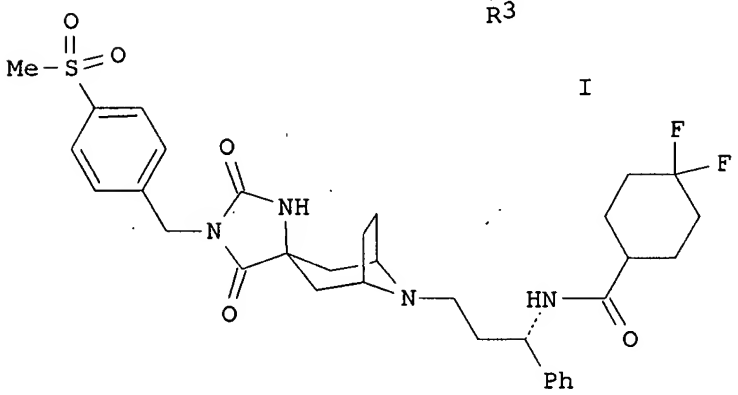
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006060919	A1	20060615	WO 2005-CA1878	20051209

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-634266P P 20041209
US 2005-693051P P 20050623
OTHER SOURCE(S): MARPAT 145:62897
GI



I



II

AB Spiro compds. according to formula (I) are claimed: wherein R1 = NR7R9; R2 = (un)substituted C1-10 alkyl, C2-10 alkenyl, 3-10 membered heterocycle, etc.; R3 = H, (un)substituted C1-10 alkyl or C6-12 aryl; R7 = H, (un)substituted C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl; R9 = H or (un)substituted C1-10-alkyl; and ring A represents a 5 or 6 membered heteroring substituted once or twice with a keto substituent. These compds. and their pharmaceutical acceptable salts are used in combinations or in pharmaceutical compns. and are useful in the modulation of CCR5 chemokine receptor activity (no data given). I are useful in the prevention or treatment of certain inflammatory diseases, immunoregulatory diseases, organ transplantation reactions and in the prevention and treatment of infectious diseases such as HIV infections. Preparation of I is exemplified. For example, II was prepared from 4,4-difluorocyclohexanecarboxylic acid ((S)-3-oxo-1-phenylpropyl)amide and 3-(4-methanesulfonylbenzyl)bicyclo[3.2.1]-1α,3,8-triazaspiro[4.5]dodecan-2,4-dione hydrochloride (preparation given).

IT 497223-28-6, TAK-652
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(addnl. therapeutic agent; preparation of spirotropane compds. and therapeutic use as modulators of chemokine receptor activity)

RN 497223-28-6 CAPLUS

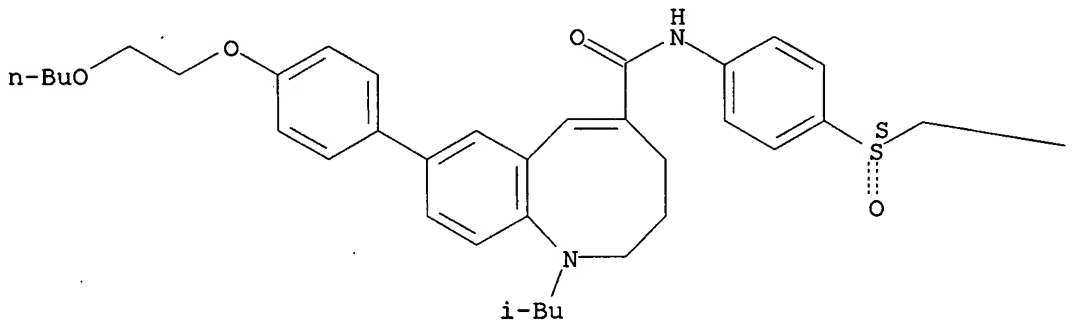
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

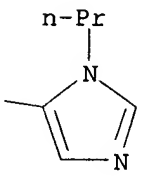
CM 1

CRN 497223-25-3
CMF C41 H52 N4 O4 S

Absolute stereochemistry. Rotation (-).

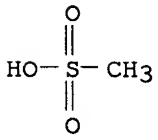
PAGE 1-A





CM 2

CRN 75-75-2
CMF C H4 O3 S



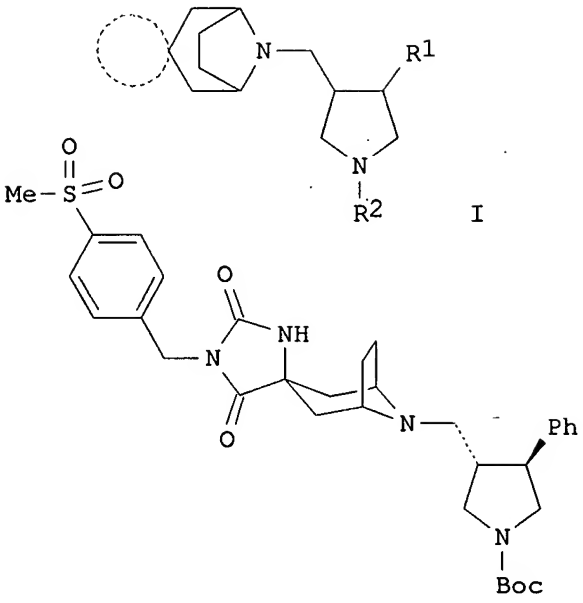
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:558325 CAPLUS
DOCUMENT NUMBER: 145:62894
TITLE: Preparation of spirotropane compounds and methods for the modulation of chemokine receptor activity to block cellular entry of HIV
INVENTOR(S): Chan Chun Kong, Laval; Moinet, Christophe; Courchesne, Marc; Vaillancourt, Louis; Bubenik, Monica
PATENT ASSIGNEE(S): Virochem Pharma Inc., Can.
SOURCE: PCT Int. Appl., 153 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006060918	A1	20060615	WO 2005-CA1877	20051209

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-634257P P 20041209
OTHER SOURCE(S): MARPAT 145:62894
GI



I

AB Compds. according to formula I (wherein the R1= (un)substituted alkyl, alkenyl, etc.; R2 = H, cycloalkylcarbonyl, ester, etc.; and A = a 5 or 6 membered heteroring involving a nitrogen or oxygen atom and one or two keto substituent) are claimed. These compds. and their pharmaceutical acceptable salt are used in combinations or pharmaceutical compns. and are useful in modulation of CCR5 chemokine receptor activity and blocking cellular entry of HIV (no biol. data given). Preparation of I is exemplified. For example, II was prepared from 3-(4-methanesulfonylbenzyl)bicyclo[3.2.1]-1a,3,8-triazaspiro[4.5]dodecan-2,4-dione hydrochloride (preparation given) and (3R,4S)-3-formyl-4-phenylpyrrolidine-1-carboxylic acid tert-Bu ester (preparation given).

IT 497223-28-6, TAK-652
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(addnl. therapeutic agent; preparation of spirotropane compds. and methods for modulation of chemokine receptor activity to block cellular entry of HIV)

RN 497223-28-6 CAPLUS

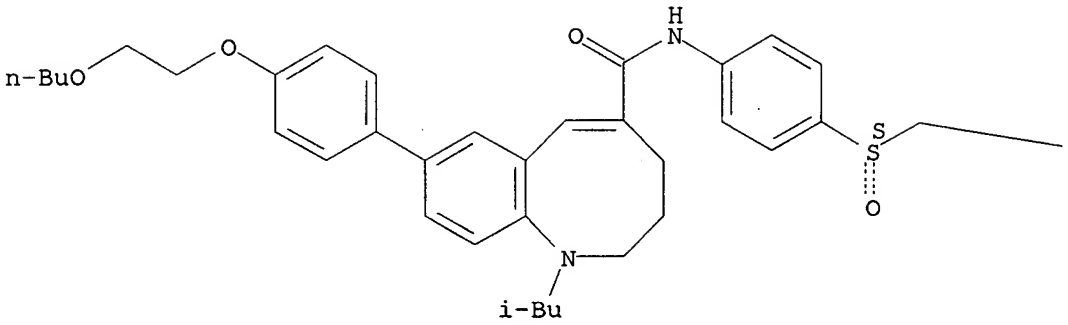
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

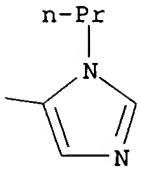
CRN 497223-25-3
CMF C41 H52 N4 O4 S

Absolute stereochemistry. Rotation (-).

PAGE 1-A

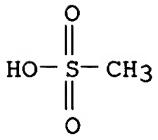


PAGE 1-B



CM 2

CRN 75-75-2
CMF C H4 O3 S



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:542810 CAPLUS
DOCUMENT NUMBER: 145:14785
TITLE: Solid preparation containing surface modifier
INVENTOR(S): Uchiyama, Yoshihiro; Yoshinari, Tomohiro; Fukuta, Makoto
PATENT ASSIGNEE(S): Takeda Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006059716	A1	20060608	WO 2005-JP22187	20051202

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2004-350972 A 20041203
OTHER SOURCE(S): MARPAT 145:14785

AB Disclosed is a medical drug, in particular, solid prepns. containing a medicinal ingredient with high tendency toward gelation, characterized by simultaneously containing a surface modifier and an acid or base. This characteristic realizes improvement to the disintegration easiness, production efficiency and stability of the solid prepns. containing the above medicinal ingredient. For example, tablets were prepared from (S)-8-[4-(2-butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide monomethanesulfonate, mannitol, citric acid, silica (Aerosil) as a surface modifier, crystalline cellulose, hydroxypropyl cellulose, sodium croscarmellose, talc, and magnesium stearate. The tablet showed improved disintegration property and storage stability.

IT 497223-28-6
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(solid preparation containing active ingredients with high gelation tendency, surface modifier, and acid or base)

RN 497223-28-6 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

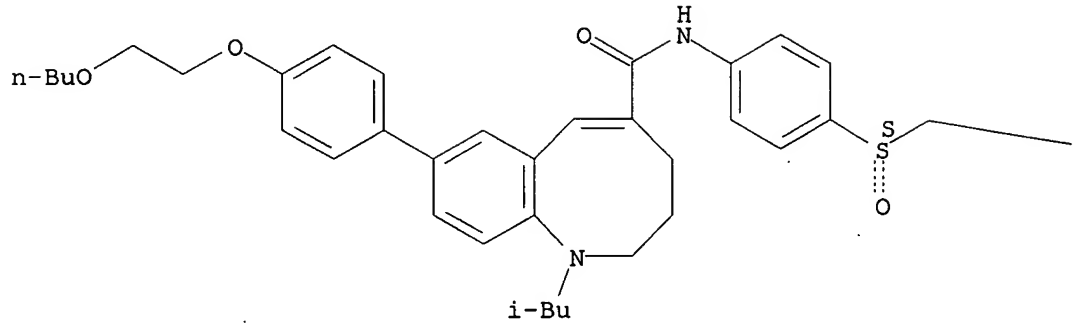
CM 1

CRN 497223-25-3

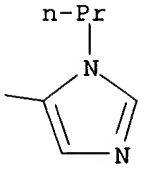
CMF C41 H52 N4 O4 S

Absolute stereochemistry. Rotation (-).

PAGE 1-A

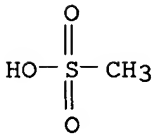


PAGE 1-B



CM 2

CRN 75-75-2
CMF C H4 O3 S



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:184008 CAPLUS
DOCUMENT NUMBER: 144:432675
TITLE: Highly Potent and Orally Active CCR5 Antagonists as Anti-HIV-1 Agents: Synthesis and Biological Activities of 1-Benzazocine Derivatives Containing a Sulfoxide Moiety
AUTHOR(S): Seto, Masaki; Aikawa, Katsuji; Miyamoto, Naoki; Aramaki, Yoshio; Kanzaki, Naoyuki; Takashima, Katsunori; Kuze, Yoji; Iizawa, Yuji; Baba, Masanori; Shiraishi, Mitsuru
CORPORATE SOURCE: Pharmaceutical Research Division, Takeda Pharmaceutical Company Limited, 2-17-85 Jusohonmachi, Yodogawa-ku, Osaka, 532-8686, Japan
SOURCE: Journal of Medicinal Chemistry (2006), 49(6), 2037-2048
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:432675
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Chemical modification was performed on the orally bioavailable and potent CCR5 antagonist sulfoxide compound I, mainly focusing on replacement of the [6,7]-fused 1-benzazepine nucleus. Ring-expanded [6,8]-, [6,9]-, and [6,10]-fused compds. containing S-sulfoxide moieties were prepared and evaluated for biol. activities which led to 1-benzazocine and 1-benzazonine compds. that exhibited potent inhibitory activities. 1-Benzazocine compds. possessing the S-sulfoxide moiety showed greater potency than I in a fusion assay. Further investigation in a multi-round infection assay showed that the 1-isobutyl-1-benzazocine compound II, containing the S-[[(1-propyl-1H-imidazol)-5-yl]methyl]sulfinyl group, showed the most potent anti-HIV-1 activity. II (TAK-652) also inhibited the replication of six macrophage-tropic HIV-1 clin. isolates in peripheral blood mononuclear cells. It was also absorbed after oral administration in rats, dogs, and monkeys and was thus selected as a clin. candidate. The synthesis and biol. activity of II and derivs. are described.

IT 497223-28-6P 497223-60-6P 497250-39-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of CC chemokine receptor 5 antagonistic chiral sulfoxide-containing benzazocines as anti-HIV-1 agents)

RN 497223-28-6 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

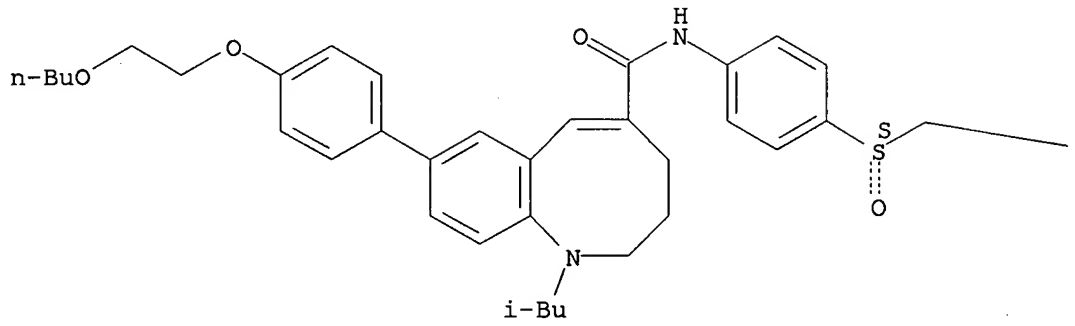
CM 1

CRN 497223-25-3

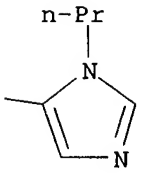
CMF C41 H52 N4 O4 S

Absolute stereochemistry. Rotation (-).

PAGE 1-A

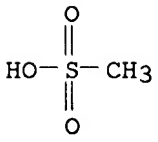


PAGE 1-B



CM 2

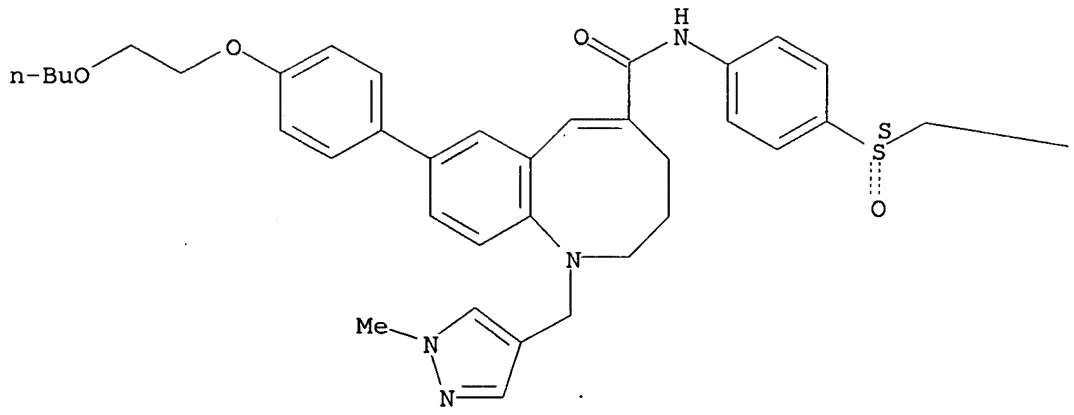
CRN 75-75-2
CMF C H4 O3 S



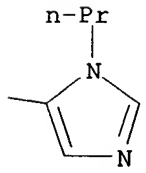
RN 497223-60-6 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-[(1-methyl-1H-pyrazol-4-yl)methyl]-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



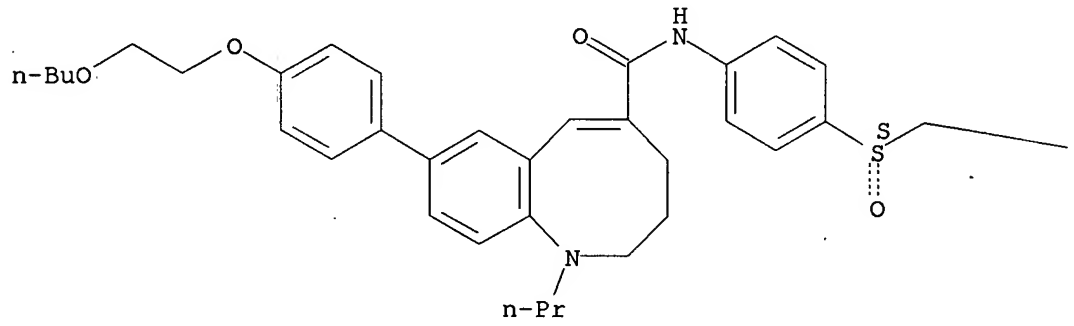
PAGE 1-B

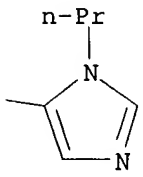


RN 497250-39-2 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-propyl-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A





REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:156018 CAPLUS
DOCUMENT NUMBER: 145:137304
TITLE: TAK-652, a novel CCR5 inhibitor, has favourable drug interactions with other antiretrovirals in vitro
AUTHOR(S): Tremblay, Cecile L.; Giguel, Francoise; Chou, Ting-Chao; Dong, Huajin; Takashima, Katsunori; Hirsch, Martin S.
CORPORATE SOURCE: Massachusetts General Hospital, Infectious Diseases Unit, Harvard Medical School, Cambridge, MA, USA
SOURCE: Antiviral Therapy (2005), 10(8), 967-968
CODEN: ANTHFA; ISSN: 1359-6535
PUBLISHER: International Medical Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB TAK-652 is a newly developed small mol., orally bioavailable CCR5 antagonist with potent in vitro anti-HIV-1 activity. Evaluation of its combination with various other antiretroviral compds., such as reverse transcriptase inhibitors, protease inhibitors, and fusion inhibitors, showed favorable and strong synergy against the multidrug-resistant isolate. Combination indexes demonstrate interactions ranging from low level antagonism at low inhibitory concns. to synergy at IC95.

IT 497223-28-6, TAK-652
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TAK-652 combination with antiretroviral agents showed favorable synergistic drug interactions in human immunodeficiency virus-1 infected cells of patient)

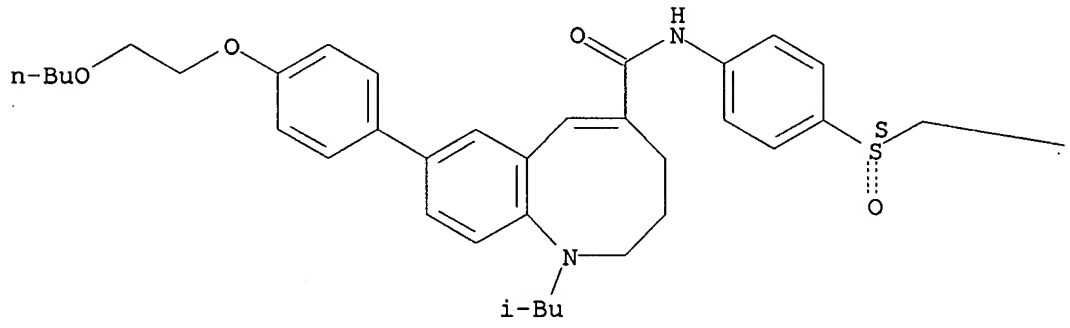
RN 497223-28-6 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

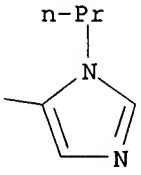
CM 1

CRN 497223-25-3
CMF C41 H52 N4 O4 S

Absolute stereochemistry. Rotation (-).

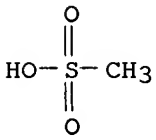
PAGE 1-A





CM 2

CRN 75-75-2
CMF C H4 O3 S



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1290185 CAPLUS
DOCUMENT NUMBER: 144:27595
TITLE: Crystal of pharmaceutical compound containing 1-benzazocine-5-carboxamide derivative, and preparation thereof
INVENTOR(S): Sugimoto, Ikutaro; Iwano, Norio
PATENT ASSIGNEE(S): Takeda Pharmaceutical Company Limited, Japan
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005116013	A1	20051208	WO 2005-JP9751	20050527

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2004-158842 A 20040528

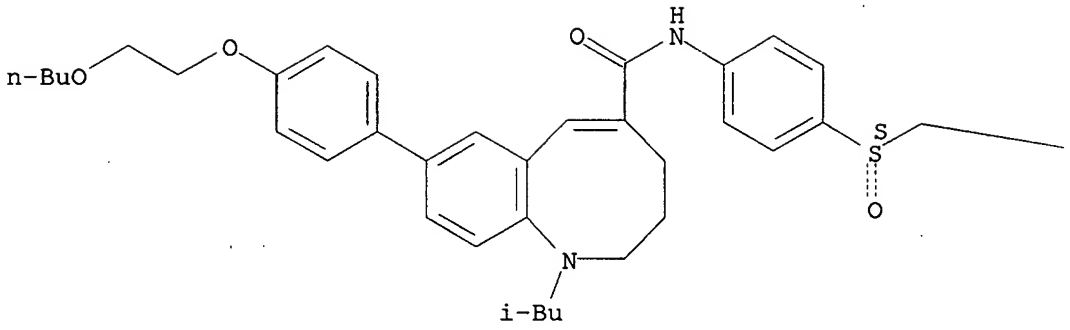
AB Disclosed is a crystal of (S)-8-[4-(2-butoxyethoxy)phenyl]-1-isobutyl-N-(4-{[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl}phenyl)-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide (I). A method of preparation of the crystal of I, and method for preparation of I methanesulfonate are also disclosed. Thus, crystal of I was prepared from 8-[4-(2-butoxyethoxy)phenyl]-1-isobutyl-1,2,3,4-tetrahydro-1-benzoazocine-5-carboxylic acid and 4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenylamine for making a tablet.

IT 497223-25-3P 497223-28-6P
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(crystal of 1-benzazocine-5-carboxamide derivative, and preparation thereof)

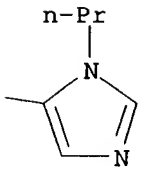
RN 497223-25-3 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



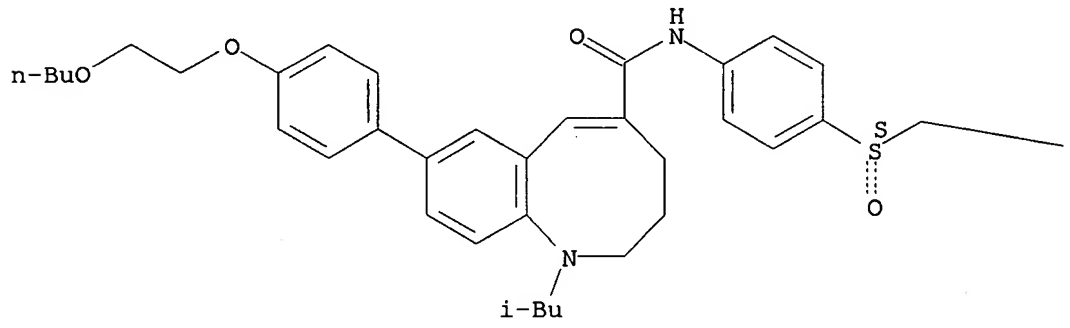
RN 497223-28-6 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

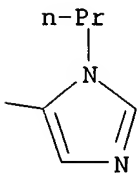
CM 1

CRN 497223-25-3
CMF C41 H52 N4 O4 S

Absolute stereochemistry. Rotation (-).

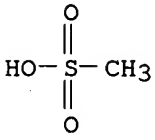
PAGE 1-A





CM 2

CRN 75-75-2
CMF C H4 O3 S



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1256967 CAPLUS
DOCUMENT NUMBER: 144:368023
TITLE: CCR5: a target for therapeutic intervention of HIV-1 infection
AUTHOR(S): Mitsuya, Hiroaki
CORPORATE SOURCE: Dep. of Infectious Diseases, Dep. of Hematology, School of Medicine, Kumamoto University, Japan
SOURCE: Jikken Igaku (2005), 23(17), 2726-2731
CODEN: JIIGEF; ISSN: 0288-5514
PUBLISHER: Yodosha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review on human immunodeficiency virus-1 (HIV-1) invasion inhibitors and chemokine receptor antagonists, discussing (1) gp41 targeted inhibitors T-20 and T-1249 and CD4 binding inhibitors PRO542 and TNX-355 and anti-CXCR4 agents, (2) CCR5 antagonists maraviroc, aplaviroc, vicraviroc and TAK-652 and (3) structural anal. of CCR5 and CCR5 antagonist binding.

IT 497223-28-6, TAK 652
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CCR5 as a target for therapeutic intervention of HIV-1 infection)

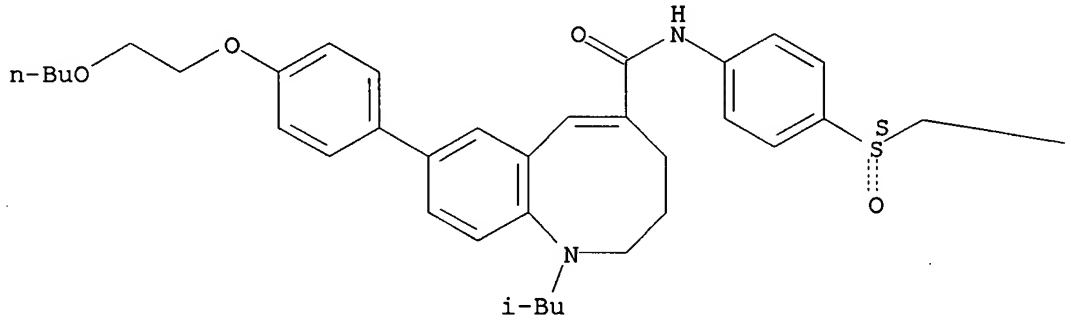
RN 497223-28-6 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

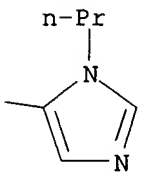
CM 1

CRN 497223-25-3
CMF C41 H52 N4 O4 S

Absolute stereochemistry. Rotation (-).

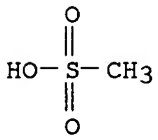
PAGE 1-A





CM 2

CRN 75-75-2
CMF C H4 O3 S



L5 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1201922 CAPLUS
DOCUMENT NUMBER: 144:16502
TITLE: TAK-652 inhibits CCR5-mediated human immunodeficiency virus type 1 infection in vitro and has favorable pharmacokinetics in humans
AUTHOR(S): Baba, Masanori; Takashima, Katsunori; Miyake, Hiroshi; Kanzaki, Naoyuki; Teshima, Koichiro; Wang, Xin; Shiraishi, Mitsuru; Iizawa, Yuji
CORPORATE SOURCE: Division of Antiviral Chemotherapy, Center for Chronic Viral Diseases, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, 890-8544, Japan
SOURCE: Antimicrobial Agents and Chemotherapy (2005), 49(11), 4584-4591
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The first small-mol. CCR5 antagonist, TAK-779, could not be developed as an anti-human immunodeficiency virus type (anti-HIV-1) agent because of its poor oral bioavailability. TAK-652 is an orally bioavailable TAK-779 derivative with potent anti-HIV-1 activity. TAK-652 inhibited the binding of RANTES (regulated on activation, normal T-cell expressed and secreted), macrophage inflammatory protein 1α (MIP-1α), and MIP-1β to CCR5-expressing cells at nanomolar concns. TAK-652 could also suppress the binding of monocyte chemotactic protein 1 (MCP-1) to CCR2b-expressing cells. However, its inhibitory effect on ligand binding to other chemokine receptors was limited. TAK-652 was active against CCR5-using (R5) HIV-1 but totally inactive against CXCR4-using (X4) HIV-1. The compound was active against R5 HIV-1 clin. isolates containing reverse transcriptase and protease inhibitor-resistant mutations, with a mean 50% effective concentration (EC50) and EC90 of 0.061 and 0.25 nM, resp. In addition, recombinant R5 viruses carrying different subtype (A to G) envelope proteins were equally susceptible to TAK-652. A single oral administration of TAK-652 up to 100 mg was safe and well tolerated in humans. The compound displayed favorable pharmacokinetics, and its plasma concentration was 7.2 ng/mL (9.1 nM) even 24 h after the administration of 25 mg.

Thus, TAK-652 is a promising candidate as a novel entry inhibitor of HIV-1.

IT 497223-28-6, TAK 652
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TAK-652 inhibits CCR5-mediated HIV-1 infection in vitro and has favorable pharmacokinetics in humans)

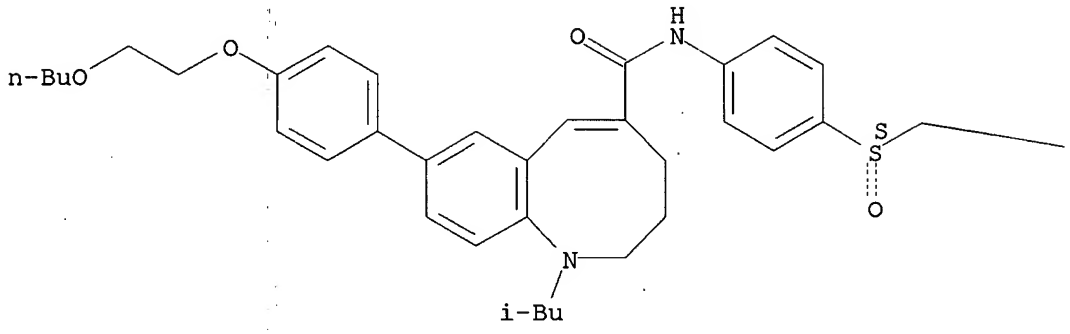
RN 497223-28-6 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

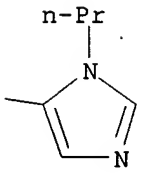
CRN 497223-25-3
CMF C41 H52 N4 O4 S

Absolute stereochemistry. Rotation (-).

PAGE 1-A

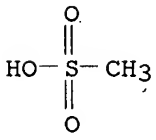


PAGE 1-B



CM 2

CRN 75-75-2
CMF C H4 O3 S



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1042033 CAPLUS
DOCUMENT NUMBER: 143:332543
TITLE: Preparation with elevated content of drugs
INVENTOR(S): Yoshinari, Tomohiro
PATENT ASSIGNEE(S): Takeda Pharmaceutical Company Limited, Japan
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005089716	A1	20050929	WO 2005-JP5239	20050323
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2560298	A1	20050929	CA 2005-2560298	20050323
EP 1728505	A1	20061206	EP 2005-727185	20050323
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: JP 2004-87032 A 20040324
WO 2005-JP5239 W 20050323
OTHER SOURCE(S): MARPAT 143:332543

AB Disclosed is a composition for oral use, which contains a drug compound (in particular, a hardly water-soluble or water-insol. drug compound) in an elevated amount and is excellent in the absorbability of the drug compound via the digestive tract, is produced by dispersing the drug compound in an oily base and a surfactant in an amount exceeding the solubility thereof in the mixture of the oily base with the surfactant under heating, adding a polar solvent which serves as a poor solvent for the drug compound to the thus obtained dispersion, and heating the mixture to give a transparent liquid composition Further, the obtained composition is encapsulated to give a capsule preparation Thus, a composition containing (S)-(-)-8-[4-(2-butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide methanesulfonate 30, polyoxyethylene hydrogenated castor oil 102, polyethylene glycol glyceryl caprylate/caprate 102, medium-chain fatty acid triglyceride 51, and water 15 mg was formulated, and filled in a gelatin soft capsule.

IT 497223-28-6, (S)-(-)-8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide methanesulfonate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. containing elevated content of drugs)

RN 497223-28-6 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-

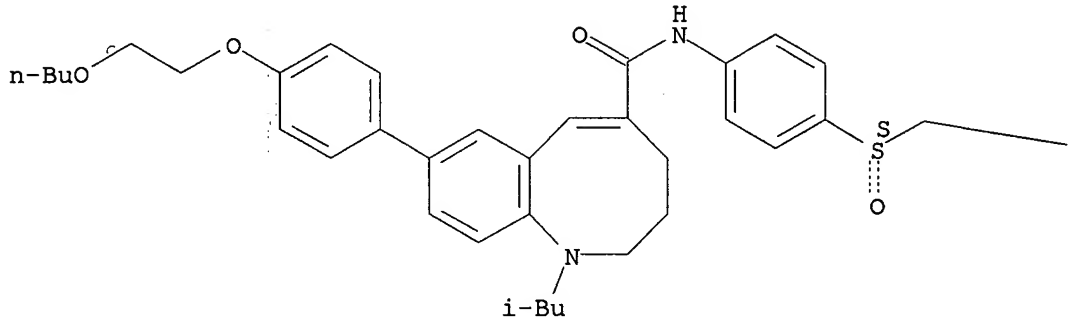
tetrahydro-1-(2-methylpropyl)-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

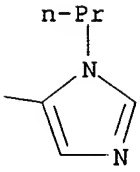
CRN 497223-25-3
CMF C41 H52 N4 O4 S

Absolute stereochemistry. Rotation (-).

PAGE 1-A

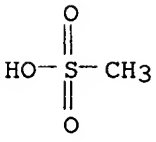


PAGE 1-B



CM 2

CRN 75-75-2
CMF C H4 O3 S



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1042031 CAPLUS
DOCUMENT NUMBER: 143:312057
TITLE: Emulsions containing hardly water-soluble drugs for oral administration
INVENTOR(S): Yoshinari, Tomohiro
PATENT ASSIGNEE(S): Takeda Pharmaceutical Company Limited, Japan
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005089714	A1	20050929	WO 2005-JP5238	20050323
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2562388	A1	20050929	CA 2005-2562388	20050323
EP 1728504	A1	20061206	EP 2005-727183	20050323
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: JP 2004-87023 A 20040324
WO 2005-JP5238 W 20050323

OTHER SOURCE(S): MARPAT 143:312057

AB It is intended to provide a medicinal composition having a high biol. availability and a process for producing the same which comprises dispersing a drug component in two or more surfactants (for example, surfactants belonging to the same series such as a long-chain fatty acid glyceride having a long-chain polyoxyethylene in its hydrophilic group with a medium-chain fatty acid glyceride having a short-chain polyoxyethylene in its hydrophilic group), adding a small amount of water thereto to give a semisolid or liquid medicinal composition in the form of a microemulsion, and producing an oral preparation such as capsules by using the same so as to form and sustain a stable microemulsion containing the drug component (in particular, a hardly water-soluble drug component) in the digestive tract. For example, (S)-(-)-8-[4-(2-butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide methanesulfonic acid salt 1 g, ethoxylated hydrogenated castor oil 3.4 g, ethoxylated caprylic/capric glyceride 3.4g, and medium-chain triglyceride 1.6 g were mixed and heated at 60° to give a dispersion. Distilled water 0.5 g was added to the dispersion to give a clear composition, which was filled into capsules.

IT 497223-28-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microemulsions containing hardly water-soluble drugs and surfactants)

RN 497223-28-6 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-

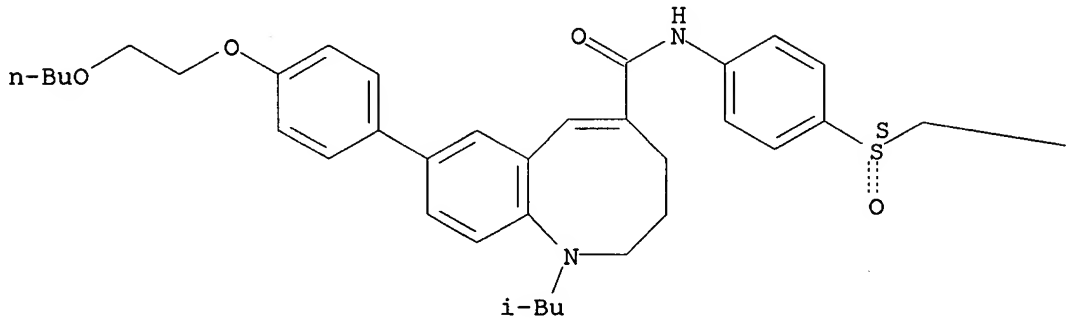
tetrahydro-1-(2-methylpropyl)-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

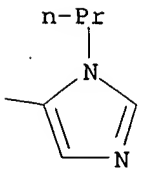
CRN 497223-25-3
CMF C41 H52 N4 O4 S

Absolute stereochemistry. Rotation (-).

PAGE 1-A

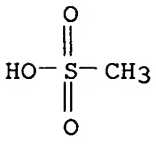


PAGE 1-B



CM 2

CRN 75-75-2
CMF C H4 O3 S



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

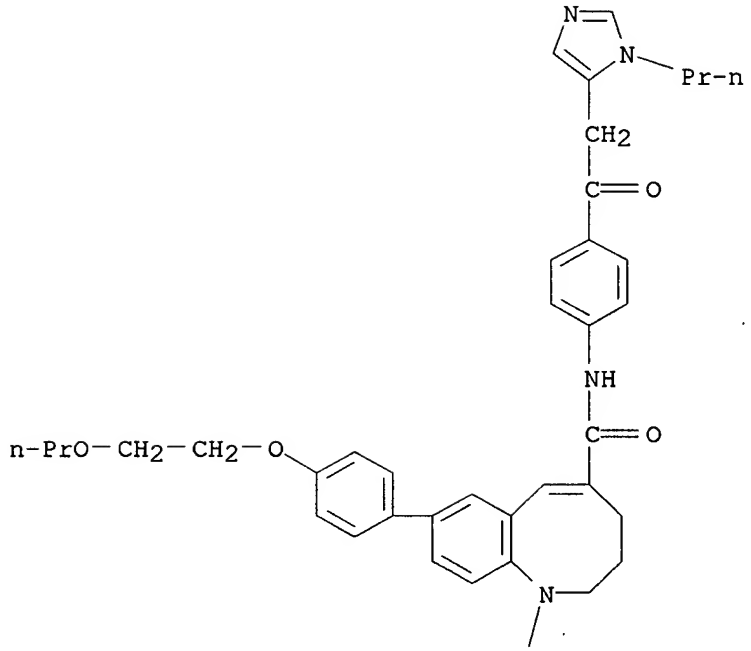
L5 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1016895 CAPLUS
DOCUMENT NUMBER: 143:415586
TITLE: G-Protein-Coupled Receptor Affinity Prediction Based on the Use of a Profiling Dataset: QSAR Design, Synthesis, and Experimental Validation
AUTHOR(S): Rolland, Catherine; Gozalbes, Rafael; Nicolaie, Eric; Paugam, Marie-France; Coussy, Laurent; Barbosa, Frederique; Horvath, Dragos; Revah, Frederic
CORPORATE SOURCE: Cerep, Rueil-Malmaison, 92500, Fr.
SOURCE: Journal of Medicinal Chemistry (2005), 48(21), 6563-6574
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A QSAR model accounting for "average" G-protein-coupled receptor (GPCR) binding was built from a large set of exptl. standardized binding data (1939 compds. systematically tested over 40 different GPCRs) and applied to the design of a library of "GPCR-predicted" compds. Three hundred and sixty of these compds. were randomly selected and tested in 21 GPCR binding assays. Positives were defined by their ability to inhibit by more than 70% the binding of reference compds. at 10 μM. A 5.5-fold enrichment in positives was observed when comparing the "GPCR-predicted" compds. with 600 randomly selected compds. predicted as "non-GPCR" from a general collection. The model was efficient in predicting strongest binders, since enrichment was greater for higher cutoffs. Significant enrichment was also observed for peptidic GPCRs and receptors not included to develop the QSAR model, suggesting the usefulness of the model to design ligands binding with newly identified GPCRs, including orphan ones.

IT 868056-98-8
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(QSAR design, synthesis, and exptl. validation of G-protein-coupled receptor affinity prediction based on use of a profiling dataset)

RN 868056-98-8 CAPLUS
CN 1-Benzazocine-5-carboxamide, 1,2,3,4-tetrahydro-1-(2-methylpropyl)-8-[4-(2-propoxyethoxy)phenyl]-N-[4-[(1-propyl-1H-imidazol-5-yl)acetyl]phenyl]-(9CI) (CA INDEX NAME)

PAGE 1-A



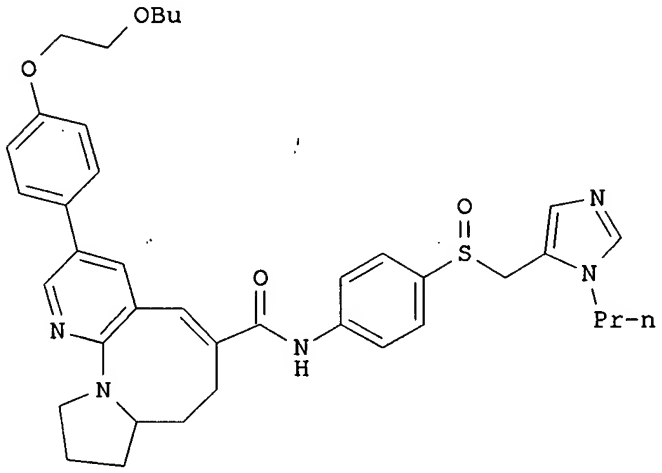
PAGE 2-A

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:675747 CAPLUS
DOCUMENT NUMBER: 141:207075
TITLE: Preparation of tricyclic compounds as CCR antagonists for treatment of HIV infection
INVENTOR(S): Shiraishi, Mitsuru; Seto, Masaki; Aikawa, Katsuji; Kanzaki, Naoyuki; Baba, Masanori
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 161 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004069834	A1	20040819	WO 2004-JP1197	20040205
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2004256531	A	20040916	JP 2004-29688	20040205
EP 1593681	A1	20051109	EP 2004-708469	20040205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006178359	A1	20060810	US 2005-544470	20050901
PRIORITY APPLN. INFO.:			JP 2003-31112 A	20030207
			WO 2004-JP1197 W	20040205

OTHER SOURCE(S): MARPAT 141:207075
GI



I

AB The title compds. with general formula of R1-W-CO-NH-Z1-Z2-R2 [wherein R1 = (un)substituted cyclyl; Z1 = (un)substituted aryl; Z2 = (un)substituted

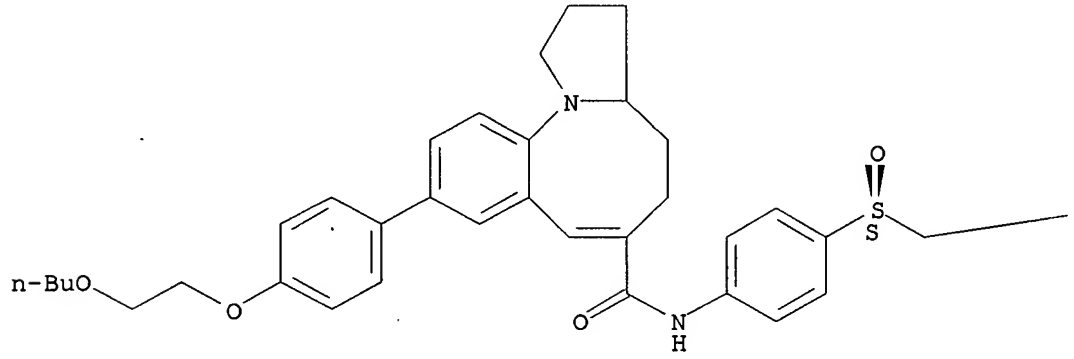
imino, alkylene, etc.; W = (un)substituted tricyclyl; R2 = (un)substituted amino, heterocyclyl, etc.] or salts or prodrugs thereof are prepared as chemokine receptors (CCR) antagonists. For example, the compound I was prepared in a multi-step synthesis. I inhibited 100% human CCR5 at 1 μM in 40 min. The compds. are useful as a preventive/therapeutic agent for HIV infection in human peripheral blood mononuclear cells, especially for AIDS (no data). Formulations containing the title compound as an active ingredient were also described.

IT 741268-80-4P 741268-88-2P
RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(drug candidate; preparation of tricyclic compds. as CCR antagonists for treatment of HIV infection)

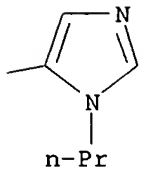
RN 741268-80-4 CAPLUS
CN Pyrrolo[1,2-a][1]benzazocine-6-carboxamide, 9-[4-(2-butoxyethoxy)phenyl]-1,2,3,3a,4,5-hexahydro-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



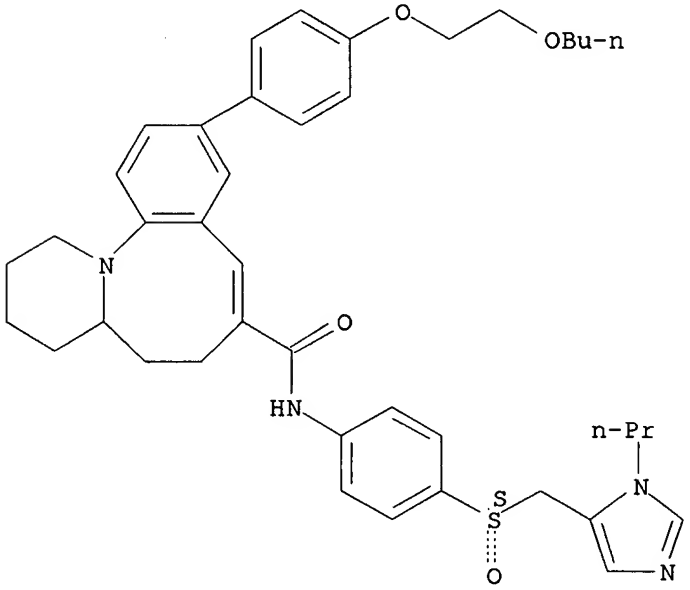
PAGE 1-B



RN 741268-88-2 CAPLUS
CN 1H-Pyrido[1,2-a][1]benzazocine-7-carboxamide, 10-[4-(2-

butoxyethoxy)phenyl]-2,3,4,4a,5,6-hexahydro-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



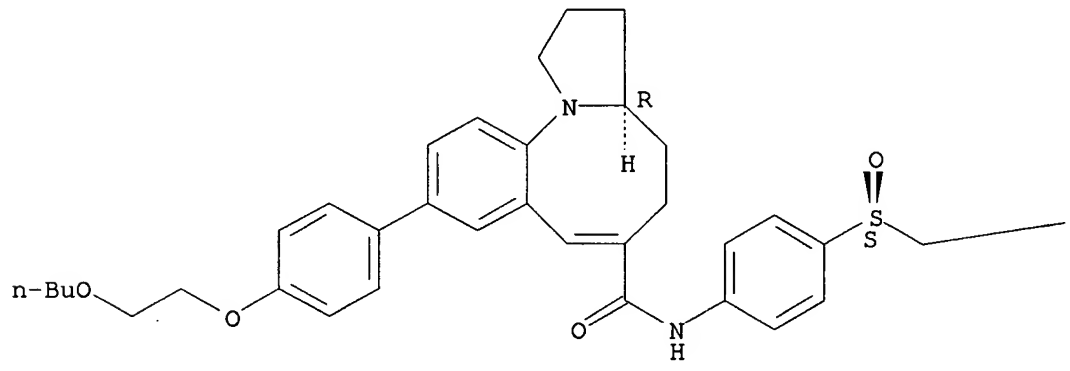
IT 741268-83-7P 741268-87-1P 741268-89-3P
741268-90-6P
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of tricyclic compds. as CCR antagonists for treatment of HIV infection)

RN 741268-83-7 CAPLUS

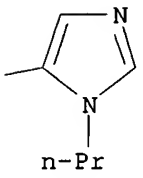
CN Pyrrolo[1,2-a][1]benzazocine-6-carboxamide, 9-[4-(2-butoxyethoxy)phenyl]-1,2,3,3a,4,5-hexahydro-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, (3aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



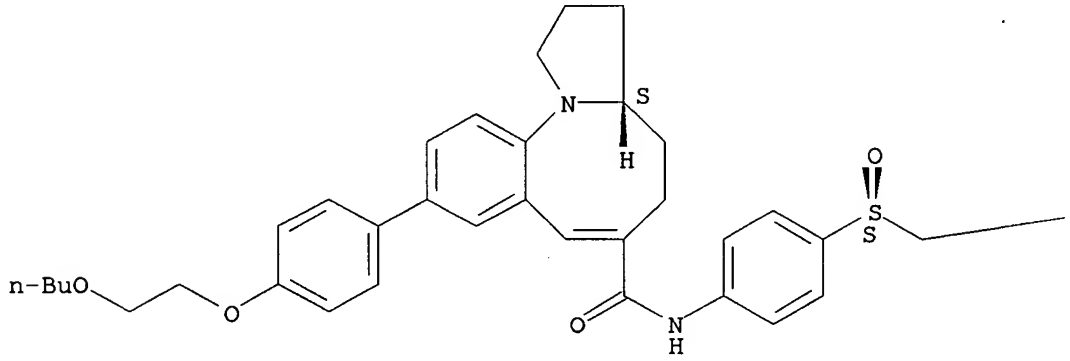
PAGE 1-B



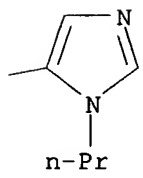
RN 741268-87-1 CAPLUS
CN Pyrrolo[1,2-a][1]benzazocine-6-carboxamide, 9-[4-(2-butoxyethoxy)phenyl]-1,2,3,3a,4,5-hexahydro-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, (3aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A

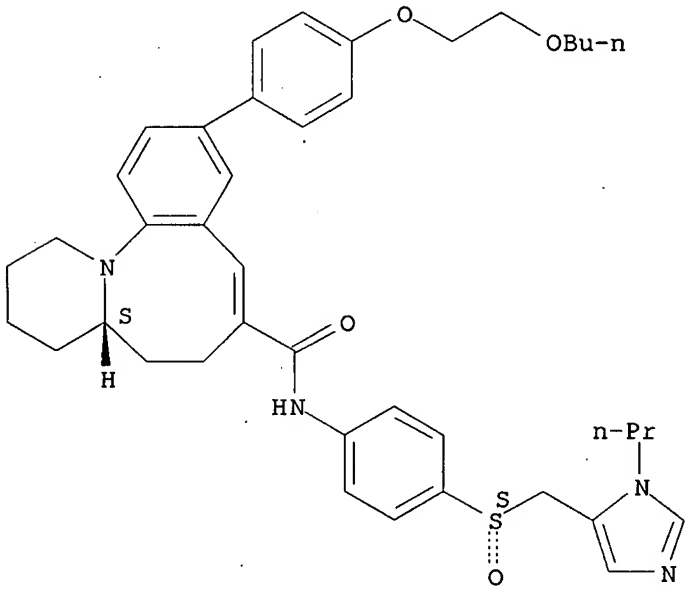


PAGE 1-B



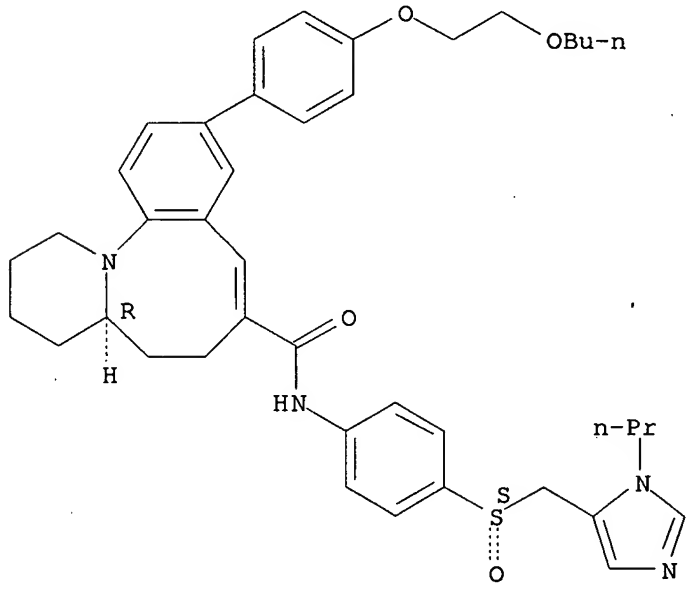
RN 741268-89-3 CAPLUS
CN 1H-Pyrido[1,2-a][1]benzazocine-7-carboxamide, 10-[4-(2-butoxyethoxy)phenyl]-2,3,4,4a,5,6-hexahydro-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, (4aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 741268-90-6 CAPLUS
CN 1H-Pyrido[1,2-a][1]benzazocine-7-carboxamide, 10-[4-(2-butoxyethoxy)phenyl]-2,3,4,4a,5,6-hexahydro-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, (4aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

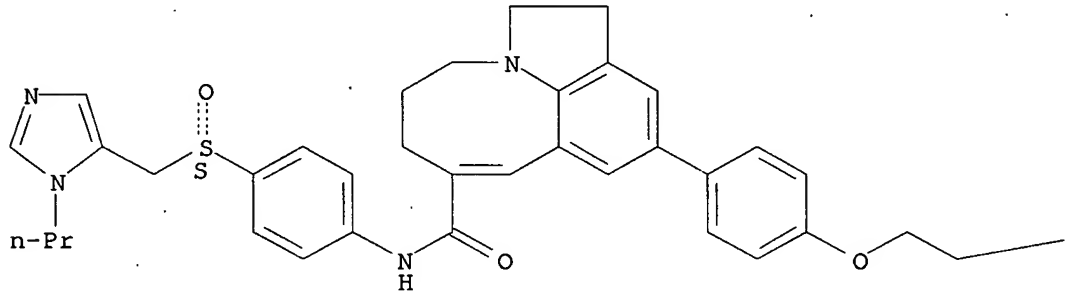


IT 741268-93-9P 741268-94-0P 741268-95-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of tricyclic compds. as CCR antagonists for treatment of HIV infection)

RN 741268-93-9 CAPLUS
CN 4H-Pyrrolo[3,2,1-kl][1]benzazocine-7-carboxamide, 10-[4-(2-butoxyethoxy)phenyl]-1,2,5,6-tetrahydro-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



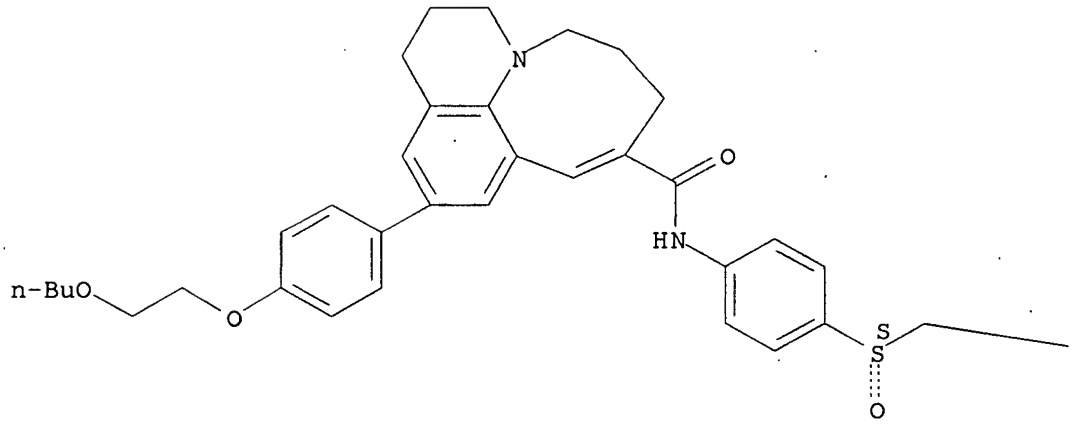
PAGE 1-B

—OBu-n

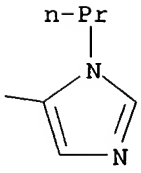
RN 741268-94-0 CAPLUS
CN 1H,5H-Pyrido[3,2,1-kl][1]benzazocine-8-carboxamide, 11-[4-(2-butoxyethoxy)phenyl]-2,3,6,7-tetrahydro-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



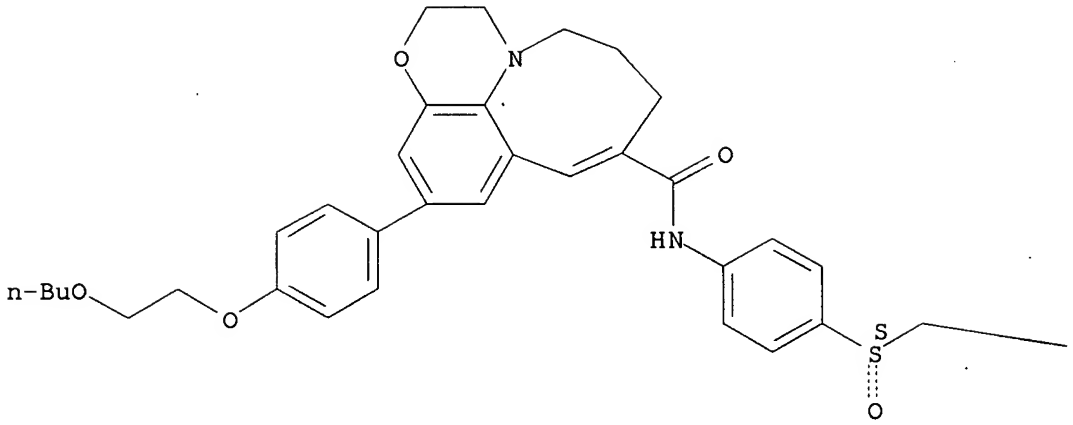
PAGE 1-B



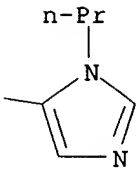
RN 741268-95-1 CAPLUS
CN 5H-1,4-Oxazino[2,3,4-kl][1]benzazocine-8-carboxamide, 11-[4-(2-butoxyethoxy)phenyl]-2,3,6,7-tetrahydro-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



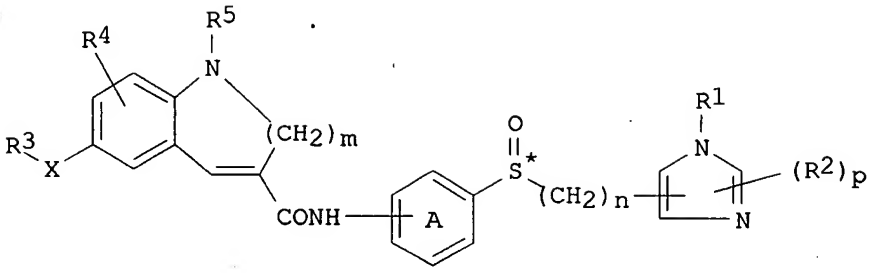
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

applicants

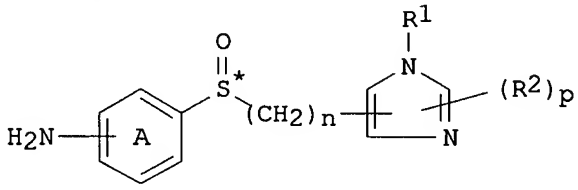
L5 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:737732 CAPLUS
DOCUMENT NUMBER: 139:246034
TITLE: Process for producing optically active imidazolylalkyl acylaminophenyl sulfoxide derivative
INVENTOR(S): Tawada, Hiroyuki; Ikemoto, Tomomi; Nishiguchi, Atsuko; Ito, Tatsuya; Adachi, Mari
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076411	A1	20030918	WO 2003-JP2840	20030311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2479071	A1	20030918	CA 2003-2479071	20030311
AU 2003213454	A1	20030922	AU 2003-213454	20030311
JP 2004123694	A	20040422	JP 2003-65258	20030311
EP 1484322	A1	20041208	EP 2003-708541	20030311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005107606	A1	20050519	US 2003-506955	20030311
CN 1649847	A	20050803	CN 2003-809855	20030311
IN 2004KN01279	A	20060421	IN 2004-KN1279	20040901
JP 2007084578	A	20070405	JP 2006-355701	20061228
PRIORITY APPLN. INFO.:			JP 2002-66809 A	20020312
			JP 2002-229802 A	20020807
			JP 2001-240750 A	20010808
			JP 2002-229532 A3	20020807
			WO 2003-JP2840 W	20030311

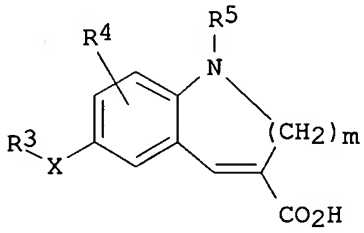
OTHER SOURCE(S): MARPAT 139:246034
GI



I



II



III

AB Disclosed is a process for producing an optically active imidazolylalkyl acylaminophenyl sulfoxide derivative (I) [wherein R1 = (un)substituted aliphatic hydrocarbon or aromatic group; R2 = halo, NO2, cyano, each (un)substituted alkyl, cycloalkyl, HO, NH2, acyl, or aromatic group, CO2H or its ester, (un)substituted SH, sulfinyl, or sulfonyl; the ring A = benzene ring optionally substituted by halo, C1-4 alkyl, C1-4-haloalkyl, C1-4 alkoxy, C1-4 haloalkoxy; n = an integer of 0-3; p = an integer of 0-2; * denotes an asym. center; R3 = 5 or 6-membered ring; R4 = H, halo each (un)substituted lower alkyl or lower alkoxy; R5 = H, each (un)substituted hydrocarbon, aromatic group, sulfonyl, or acyl, CO2H or its ester or amide; X = a bond, a divalent group consisting of 1-4 atoms in the straight chain portion] or a salt thereof, which comprises reacting an imidazolylalkyl aminophenyl sulfoxide derivative (II; R1, R2, the ring A, n, p, * = same as above) with a benzoazacycloalkenecarboxylic acid derivative (III; R3-R5, m, X = same as above) or its salt or reactive derivative This process does not cause side reactions such as racemization and Pummerer rearrangement and is industrially advantageous for the preparation of the title compds. which have CCR5 antagonistic activity (no data). Thus, 27.9 mL Et3N was added dropwise to a solution of 12.5 g 4-aminobenzenethiol in 180 mL THF, followed by adding dropwise 28.2 mL trifluoroacetic anhydride at 0-10°, and the resulting mixture was stirred at 0-5° for 0.5, treated with 30 mL tap water, and stirred at room temperature for 0.5 h to give, after workup and crystallization from n-hexane, 26.1 g 2,2,2-trifluoro-N-(4-mercaptophenyl)acetamide (IV). Et3N (29.0 mL) was added to a solution of 24.8 g IV in 99 mL MeOH, followed by adding a solution of 20.4 g 5-(chloromethyl)-1-propyl-1H-imidazole hydrochloride in 21 mL H2O at 0-20°, and the resulting mixture was stirred at 20-30° for 0.5 h to give after workup and crystallization from iso-Pr ether, 73%

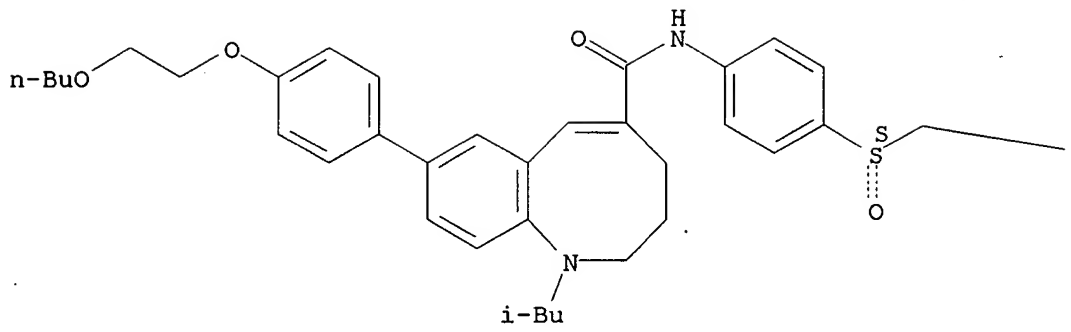
2,2,2-trifluoro-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]thio]phenyl]acetamide (V). 30% Aqueous H2O2 (16.4 g) was added to a solution of 33.1 g V in 49.7 mL at 2-30°, stirred at the same temperature for 3 h and treated with 330 mL EtOAc, followed by adding 35.9 g Na2S2O3.5 H2O at 0-10° and then dropwise 144.6 mL 6 N aqueous NaOH, and the resulting mixture was stirred at the same temperature for 0.5 h to give, after workup, 2,2,2-trifluoro-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]acetamide which was dissolved in 198.6 mL MeOH, treated with a solution of 40.0 g K2CO3 in 99.3 mL H2O and stirred at 50° for 2.5 h to give, after workup including decolorization with activated charcoal and crystallization from EtOAc, 73% 4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenylamine (VI). H2O (90 mL) was added dropwsie to a solution of 15.1 g di-p-toluoyl-D-tartaric acid (VII) and 10.3 g VI in 1,2-dimethoxyethane and stirred at room temperature overnight, followed by filtration of the precipitated crystals, washing with 50% by volume aqueous 1,2-dimethoxyethane (30 mL), vacuum-drying, recrystn. from aqueous MeCN, and vacuum-drying to give, 41.6% (-)-VI.VII diastereomer salt (99.6% de). (-)-VI.VII diastereomer salt (5 g) was extracted with 3 N aqueous HCl and 20 mL EtOAc and the aqueous layer was treated with 5 mL EtOAc 6 N aqueous NaOH to adjust pH at .apprx.9, seeded with crystals, stirred at room temperature, and filtered to give 95.4% (-)-VI (1.88 g) as a white powder. A solution of 2.56 g 7-[4-(2-butoxyethoxy)phenyl]-1-isobutyl-2,3-dihydro-1H-1-benzazepine-4-carboxylic acid in 7.5 mL THF was treated with one drop of DMF and then dropwise with 0.56 mL oxalyl chloride at room temperature, and stirred for 1 h to give a solution of the acid chloride which was added dropwsie to a solution of (-)-VI, similarly prepared from 5 g (-)-VI.VII diastereomer salt, in 17.5 mL THF and 2.85 mL Et3N at room temperature and stirred at room temperature for 1 h to give, after workup including treatment with silica gel and activated charcoal, and crystallization from ethanol-tert-Bu Me ether, 78% (-)-7-[4-(2-butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-2,3-dihydro-1H-1-benzazepine-4-carboxamide.

IT 497223-25-3P 497223-28-6P 497250-40-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of optically active imidazolylalkyl acylaminophenyl sulfoxide derivs. by amidation of optically active imidazolylalkyl aminophenyl sulfoxides with benzoazacycloalkenecarboxylic acids as CCR5 antagonists)

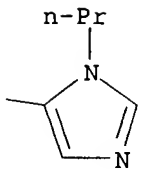
RN 497223-25-3 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



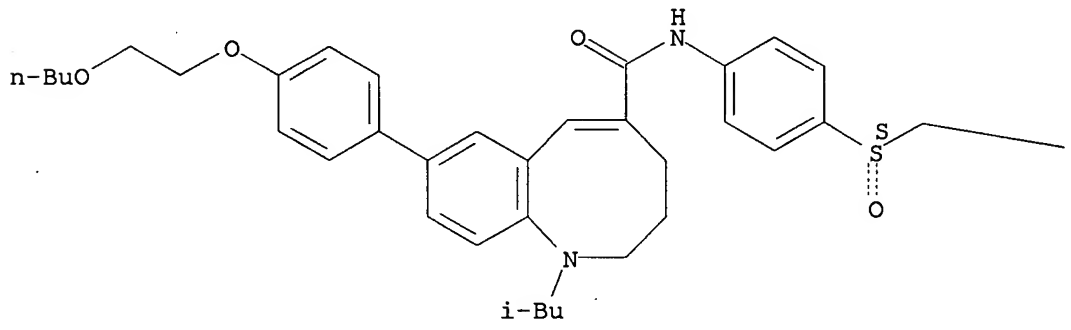
RN 497223-28-6 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

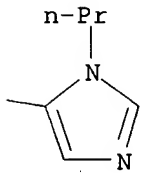
CRN 497223-25-3
CMF C41 H52 N4 O4 S

Absolute stereochemistry. Rotation (-).

PAGE 1-A

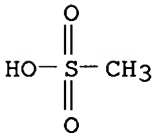


PAGE 1-B



CM 2

CRN 75-75-2
CMF C H4 O3 S



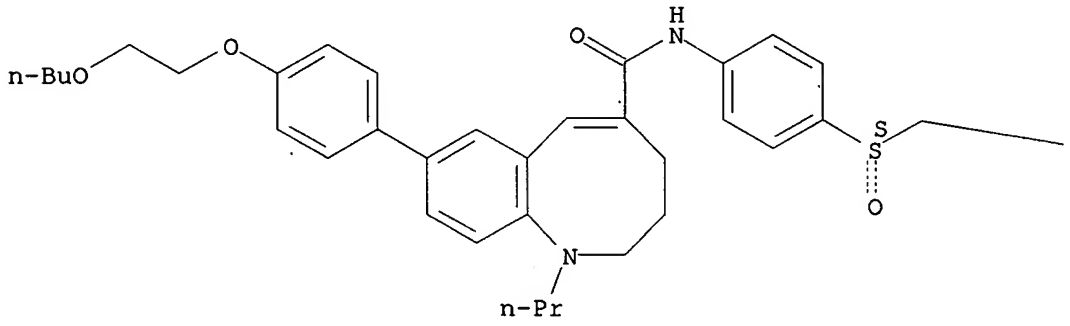
RN 497250-40-5 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-propyl-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

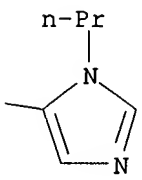
CM 1

CRN 497250-39-2
CMF C40 H50 N4 O4 S

Absolute stereochemistry. Rotation (-).

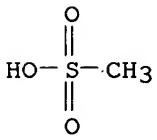
PAGE 1-A





CM 2

CRN 75-75-2
CMF C H4 O3 S



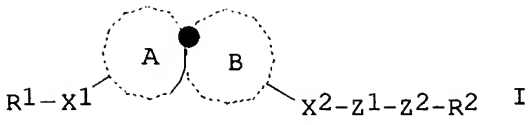
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:133258 CAPLUS
DOCUMENT NUMBER: 138:170089
TITLE: Preparation of 1-benzazocine-5-carboxamides and related bicyclic compounds as CCR-5 antagonists for use against HIV infectious and other diseases
INVENTOR(S): Shiraishi, Mitsuru; Baba, Masanori; Aikawa, Katsuji; Kanzaki, Naoyuki; Seto, Masaki; Iizawa, Yuji
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 318 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

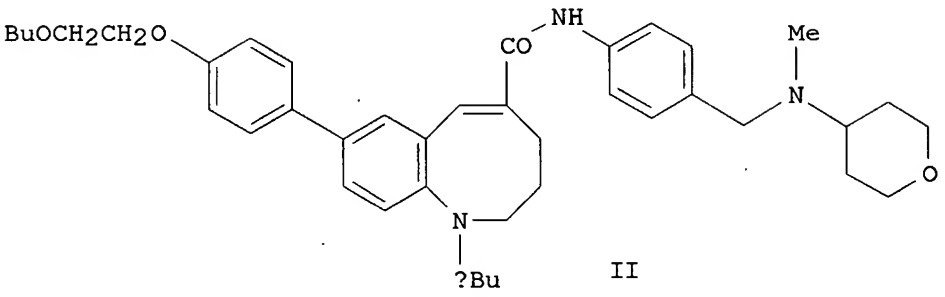
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003014105	A1	20030220	WO 2002-JP8043	20020807
WO 2003014105	A9	20031120		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2459172	A1	20030220	CA 2002-2459172	20020807
AU 2002328092	A1	20030224	AU 2002-328092	20020807
JP 2003335776	A	20031128	JP 2002-229532	20020807
EP 1423376	A1	20040602	EP 2002-762751	20020807
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE				
US 2004259876	A1	20041223	US 2004-484762	20040123
JP 2007084578	A	20070405	JP 2006-355701	20061228

PRIORITY APPLN. INFO.:
JP 2001-240750 A 20010808
JP 2002-66809 A 20020312
JP 2002-229532 A3 20020807
WO 2002-JP8043 W 20020807

OTHER SOURCE(S): MARPAT 138:170089
GI



I



II

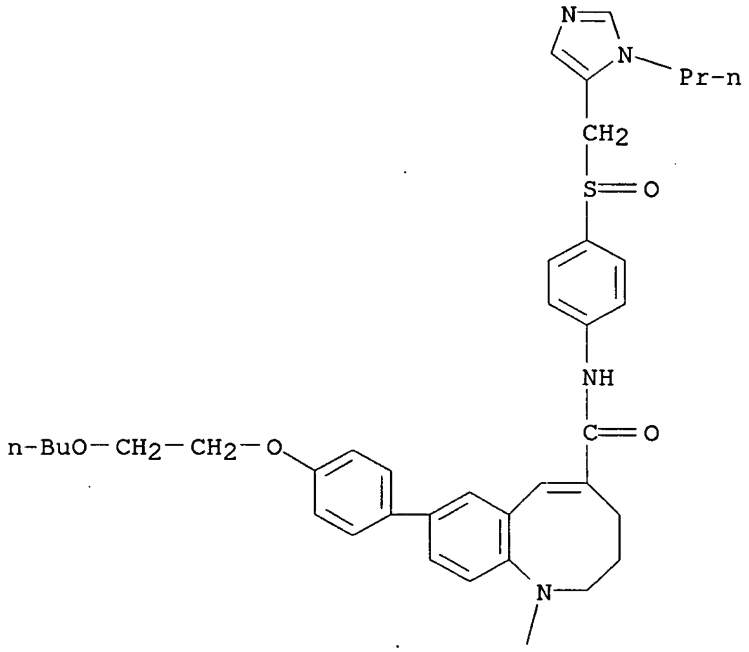
AB The present invention provides 1-benzazocine-5-carboxamides and related bicyclic compds. (shown as I or a salt thereof; variables defined below; e.g. 8-[4-(2-butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[N-methyl-N-(tetrahydropyran-4-yl)amino]methyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide (shown as II)) having a CCR antagonist activity, especially a CCR5 antagonist activity, and the use thereof. For I: R1 is a 5- to 6-membered ring group which may be substituted; X1 is a bond or bivalent chain; ring A is a 5- to 6-membered ring group which may be substituted; ring B is a 8- to 10-membered ring group which may be substituted; X2 is a bivalent chain; Z1 is a bond or bivalent cyclic ring group; Z2 is a bond or a bivalent group; and R2 is an amino group, a N-containing heterocyclic group, etc. Fifty examples of preparation of I and 63 examples of preparation of intermediates are included. For example, 8-[4-(2-butoxyethoxy)phenyl]-N-[4-[[N-methyl-N-(tetrahydropyran-4-yl)amino]methyl]phenyl]-3,4-dihydro-2H-1-benzoxocin-5-carboxamide (66 mg) was prepared by 1st adding DMF, then thionyl chloride to 8-[4-(2-butoxyethoxy)phenyl]-3,4-dihydro-2H-1-benzoxocin-5-carboxylic acid (80 mg); this mixture was added to 4-[[N-methyl-N-(tetrahydropyran-4-yl)amino]methyl]aniline (57 mg) and triethylamine in THF. CCR-5 binding inhibitory ratios (%) are tabulated for 28 examples of I at 1 μM. Six examples of pharmaceutical compns. are included.

IT 497223-17-3P, 8-[4-(2-Butoxyethoxy)phenyl]-1-propyl-N-[4-[[(1-propylimidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-21-9P, 8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-31-1P, 8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[(1-propylimidazol-2-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-35-5P, 8-[4-(2-Butoxyethoxy)phenyl]-1-propyl-N-[4-[[(1-propylimidazol-2-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-56-0P, 8-[4-(2-Butoxyethoxy)phenyl]-1-(2-methyl-3-hydroxypropyl)-N-[4-[[(1-propylimidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide
RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(drug candidate, chromatog. resolution; preparation of benzazocinecarboxamides
and related bicyclic compds. as CCR-5 antagonists for use against HIV infectious and other diseases)

RN 497223-17-3 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-propyl-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

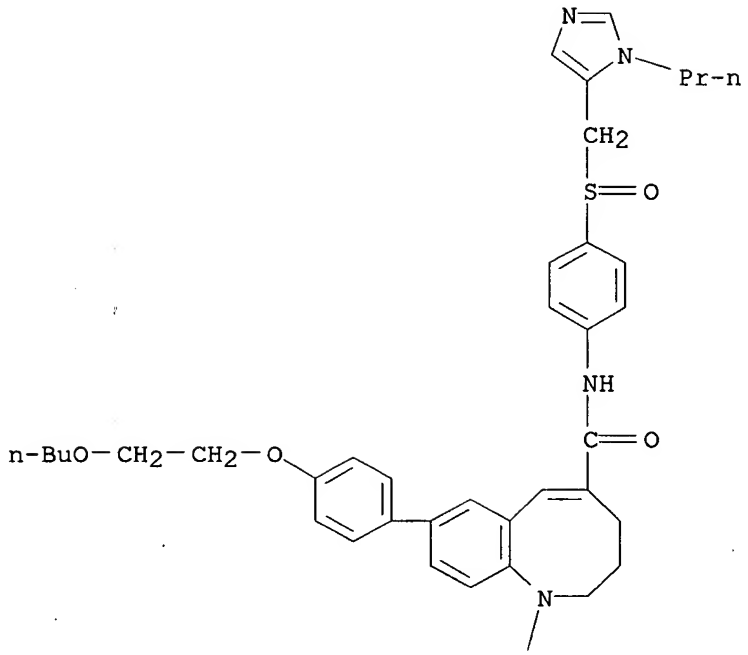
PAGE 1-A



PAGE 2-A

RN 497223-21-9 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

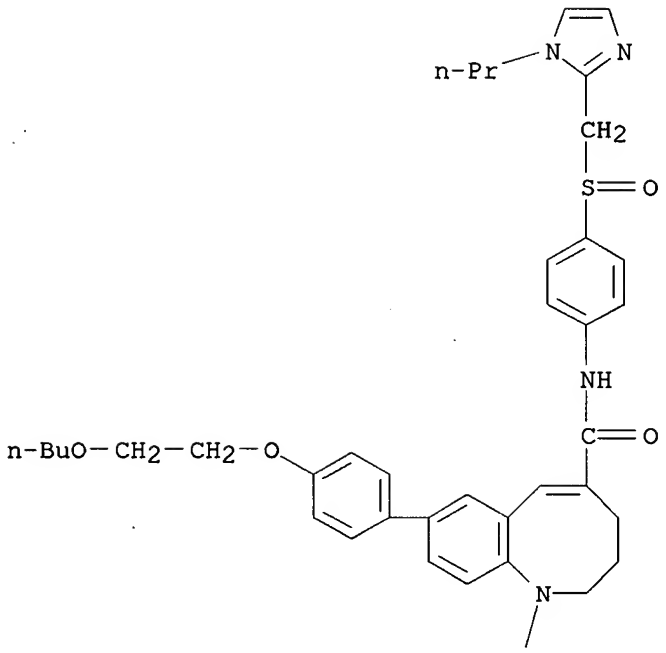
PAGE 1-A



PAGE 2-A

RN 497223-31-1 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[[(1-propyl-1H-imidazol-2-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

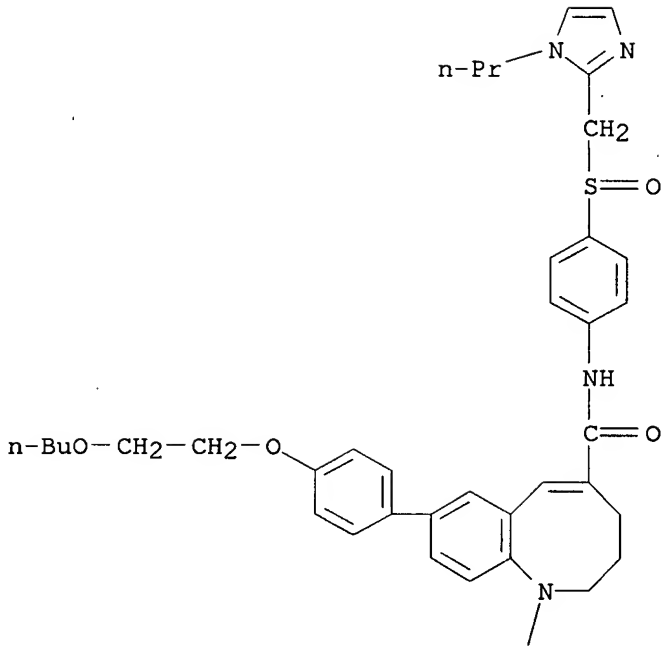
PAGE 1-A



PAGE 2-A

RN 497223-35-5 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-propyl-N-[4-[[(1-propyl-1H-imidazol-2-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

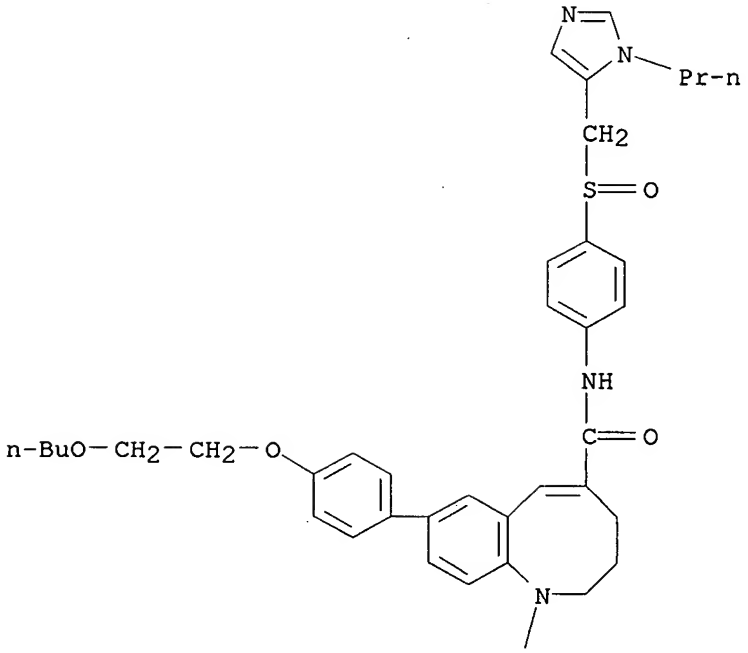
PAGE 1-A



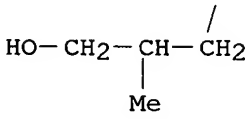
PAGE 2-A

RN 497223-56-0 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(3-hydroxy-2-methylpropyl)-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



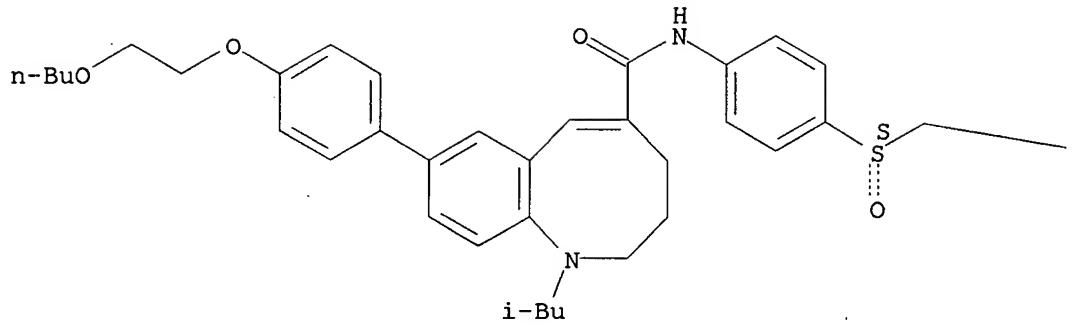
IT 497223-25-3P, (-)-8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497250-39-2P, (-)-8-[4-(2-Butoxyethoxy)phenyl]-1-propyl-N-[4-[[(1-propylimidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide
RL: PAC (Pharmacological activity); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of benzazocinecarboxamides and related bicyclic compds. as CCR-5 antagonists for use against HIV infectious and other diseases)

RN 497223-25-3 CAPLUS

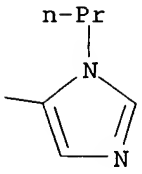
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



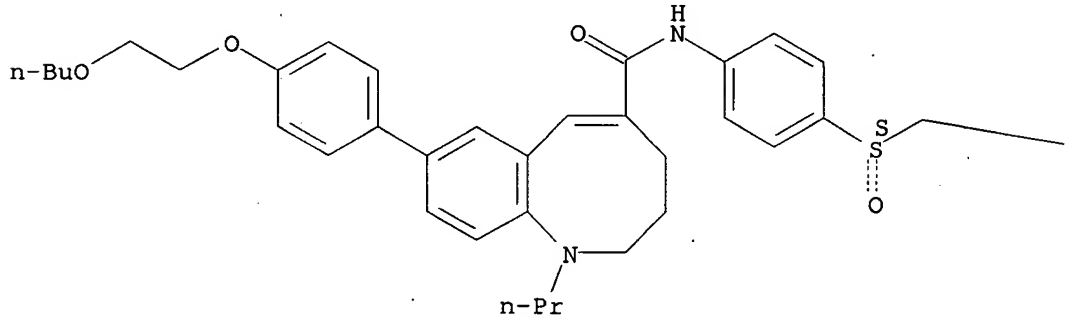
PAGE 1-B



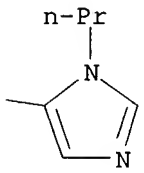
RN 497250-39-2 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-propyl-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



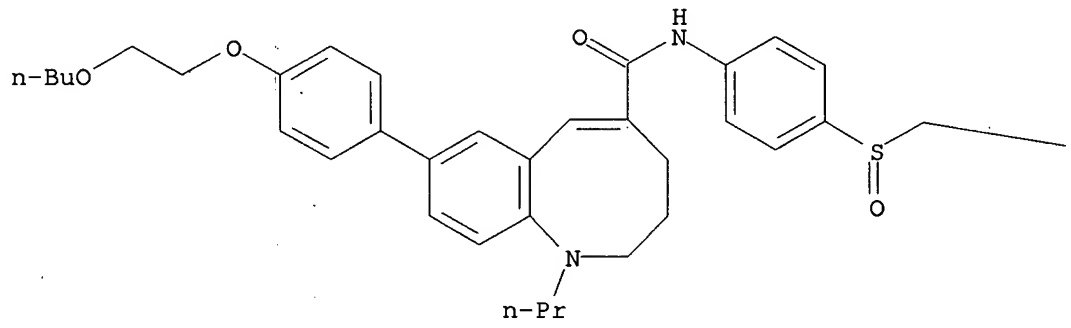
IT 497223-24-2P, (+)-8-[4-(2-Butoxyethoxy)phenyl]-1-propyl-N-[4-[[(1-propylimidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-26-4P, (+)-8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-32-2P, (+)-8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[(1-propylimidazol-2-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-33-3P, (-)-8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[(1-propylimidazol-2-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of benzazocinecarboxamides and related bicyclic compds. as CCR-5 antagonists for use against HIV infectious and other diseases)

RN 497223-24-2 CAPLUS

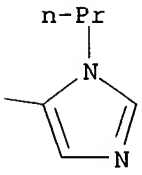
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-propyl-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

PAGE 1-A



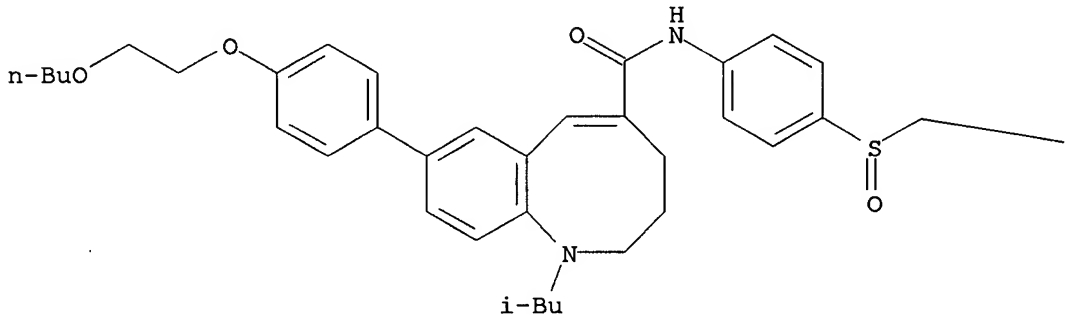
PAGE 1-B



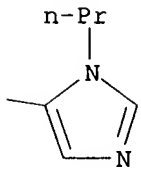
RN 497223-26-4 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

PAGE 1-A



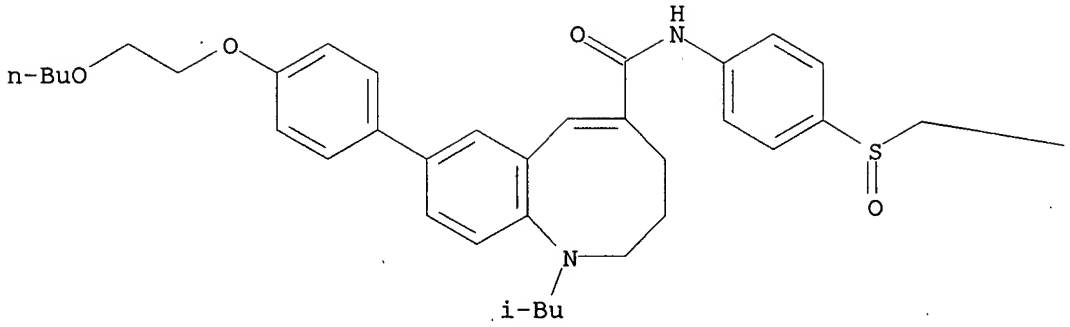
PAGE 1-B



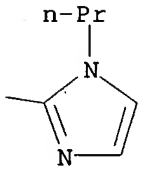
RN 497223-32-2 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[[(1-propyl-1H-imidazol-2-yl)methyl]sulfinyl]phenyl]-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

PAGE 1-A



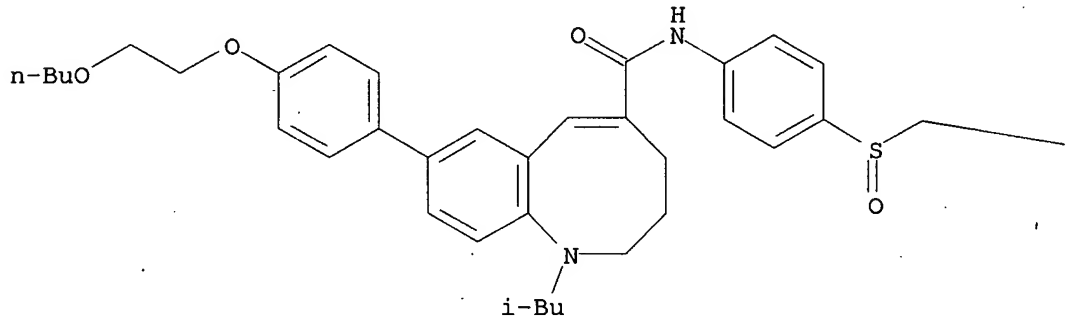
PAGE 1-B

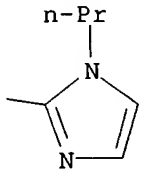


RN 497223-33-3 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[[(1-propyl-1H-imidazol-2-yl)methyl]sulfinyl]phenyl]-, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

PAGE 1-A



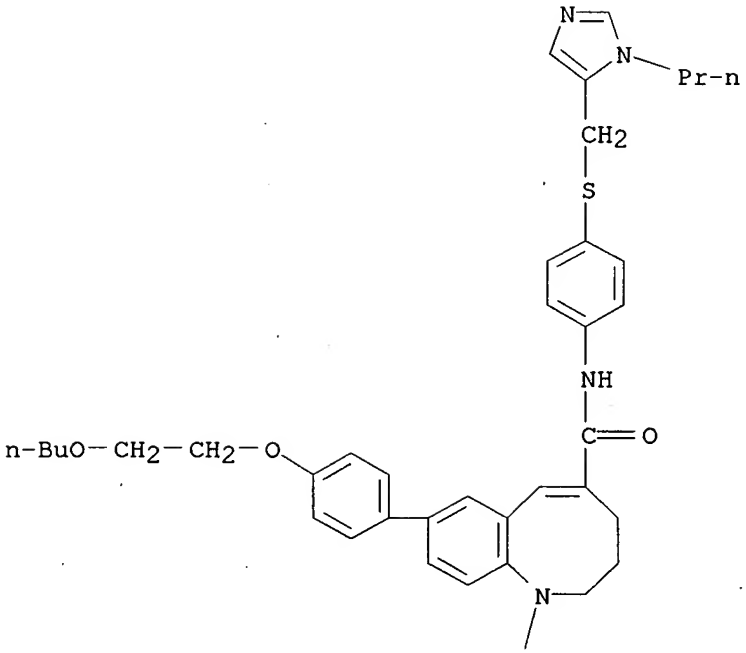


IT 497223-16-2P, 8-[4-(2-Butoxyethoxy)phenyl]-1-propyl-N-[4-[[(1-propylimidazol-5-yl)methyl]sulfanyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-20-8P, 8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfanyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-34-4P, 8-[4-(2-Butoxyethoxy)phenyl]-1-propyl-N-[4-[[(1-propylimidazol-2-yl)methyl]sulfanyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-53-7P, (-)-8-[4-(2-Butoxyethoxy)phenyl]-1-formyl-N-[4-[[(1-propylimidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-54-8P, (-)-8-[4-(2-Butoxyethoxy)phenyl]-N-[4-[[(1-propylimidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-55-9P 497223-58-2P, Ethyl 4-[2-[[[4-[[[8-[4-(2-butoxyethoxy)phenyl]-1-isobutyl-1,2,3,4-tetrahydro-1-benzazocine-5-yl]carbonyl]amino]phenyl]sulfanyl]methyl]imidazol-1-yl]butanoate 497223-64-0P, 8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[(4-methyl-1-propylimidazol-5-yl)methyl]sulfanyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-67-3P, 8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-N-[3-methyl-4-[[(1-propylimidazol-5-yl)methyl]sulfanyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-70-8P, 8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-N-[3-methyl-4-[[(4-methyl-1-propylimidazol-5-yl)methyl]sulfanyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-90-2P, 8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[[1-[4-(methylamino)-4-oxobutyl]imidazol-2-yl]methyl]sulfanyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of benzazocinecarboxamides and related bicyclic compds. as CCR-5 antagonists for use against HIV infectious and other diseases)

RN 497223-16-2 CAPLUS

CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-propyl-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]thio]phenyl]-(9CI) (CA INDEX NAME)

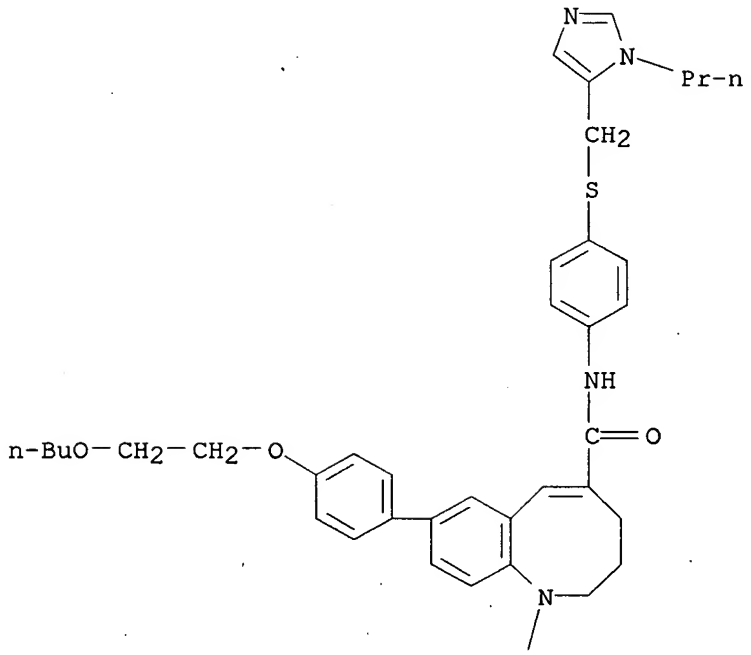
PAGE 1-A



PAGE 2-A

RN 497223-20-8 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]thio]phenyl]- (9CI) (CA INDEX NAME)

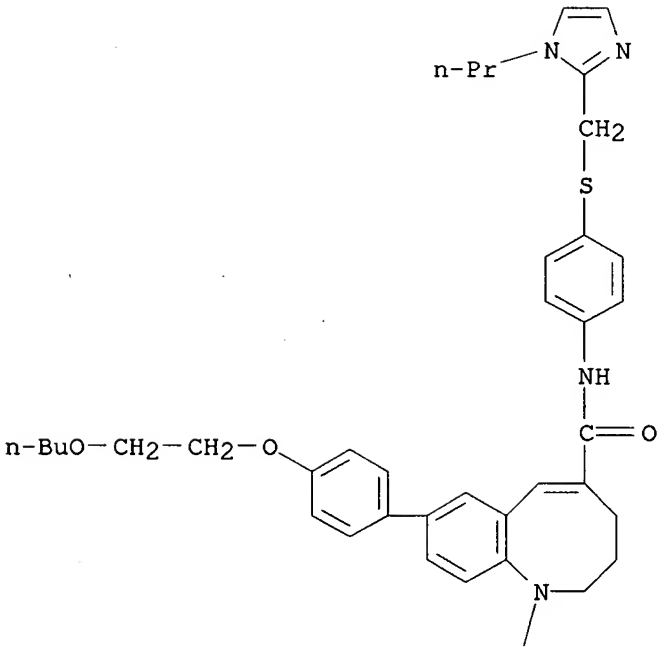
PAGE 1-A



PAGE 2-A

RN 497223-34-4 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-propyl-N-[4-[[(1-propyl-1H-imidazol-2-yl)methyl]thio]phenyl]-(9CI) (CA INDEX NAME)

PAGE 1-A

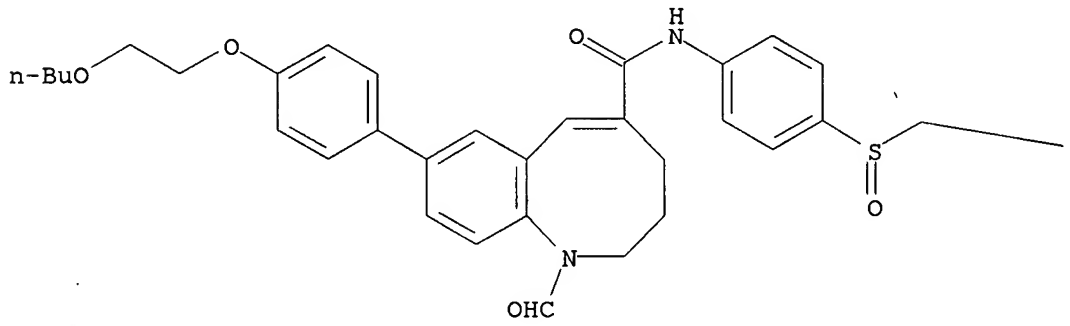


PAGE 2-A

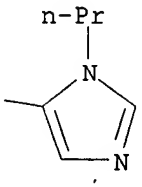
RN 497223-53-7 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1-formyl-1,2,3,4-tetrahydro-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

PAGE 1-A



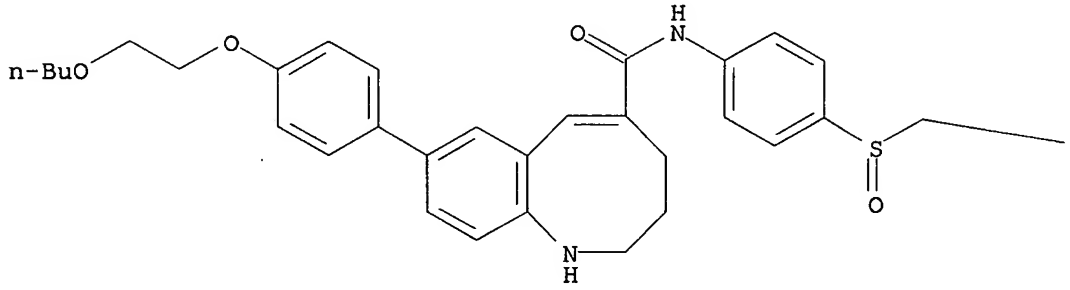
PAGE 1-B



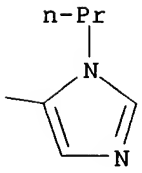
RN 497223-54-8 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

PAGE 1-A

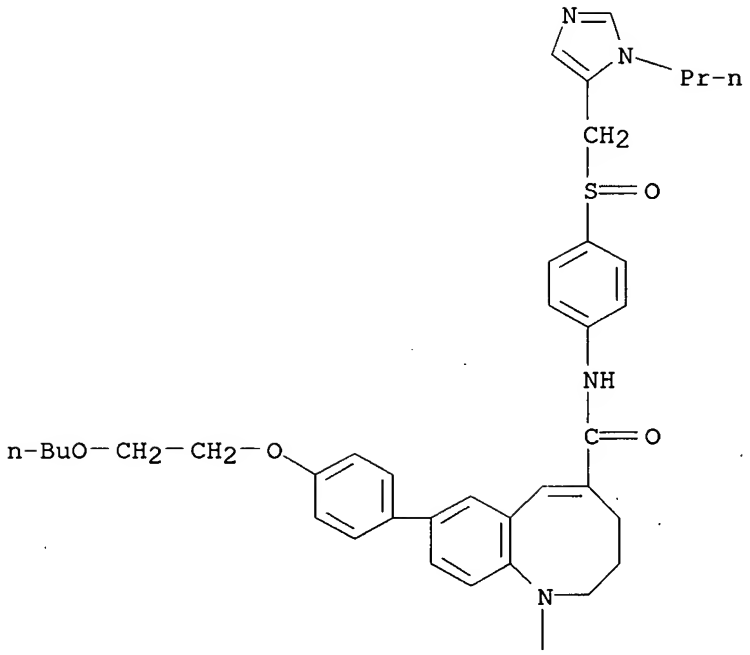


PAGE 1-B

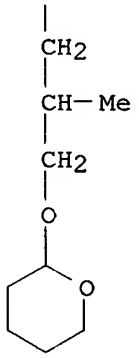


RN 497223-55-9 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-[2-methyl-3-[(tetrahydro-2H-pyran-2-yl)oxy]propyl]-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

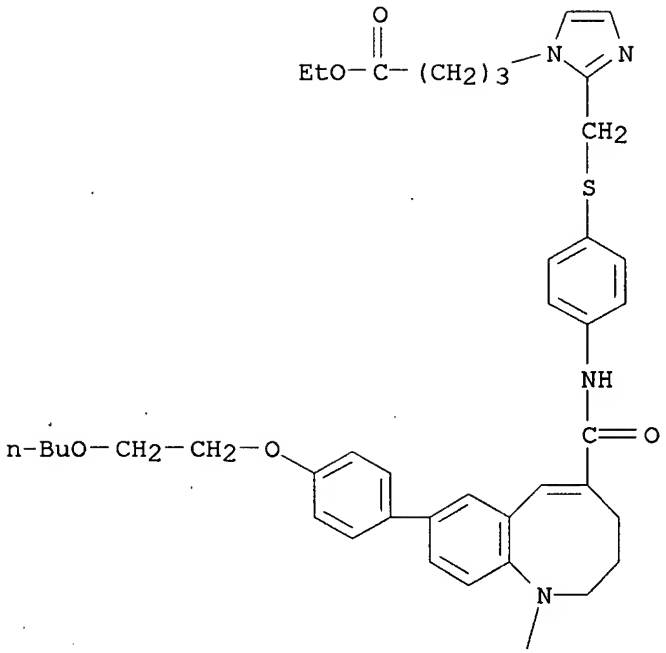


PAGE 2-A



RN 497223-58-2 CAPLUS
CN 1H-Imidazole-1-butanoic acid, 2-[[[4-[[[8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-1-benzazocin-5-yl]carbonyl]amino]phenyl]thio]methyl]-, ethyl ester (9CI) (CA INDEX NAME)

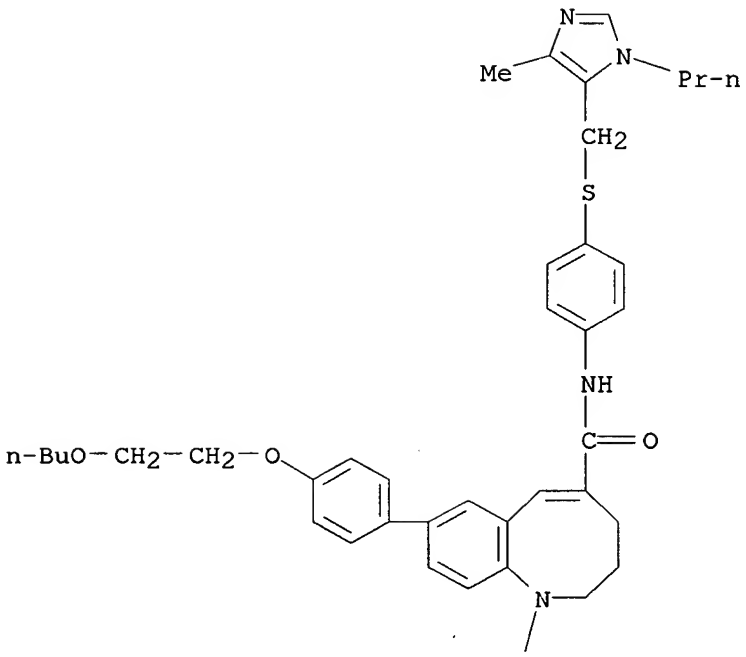
PAGE 1-A



PAGE 2-A

RN 497223-64-0 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[[(4-methyl-1-propyl-1H-imidazol-5-yl)methyl]thio]phenyl]- (9CI) (CA INDEX NAME)

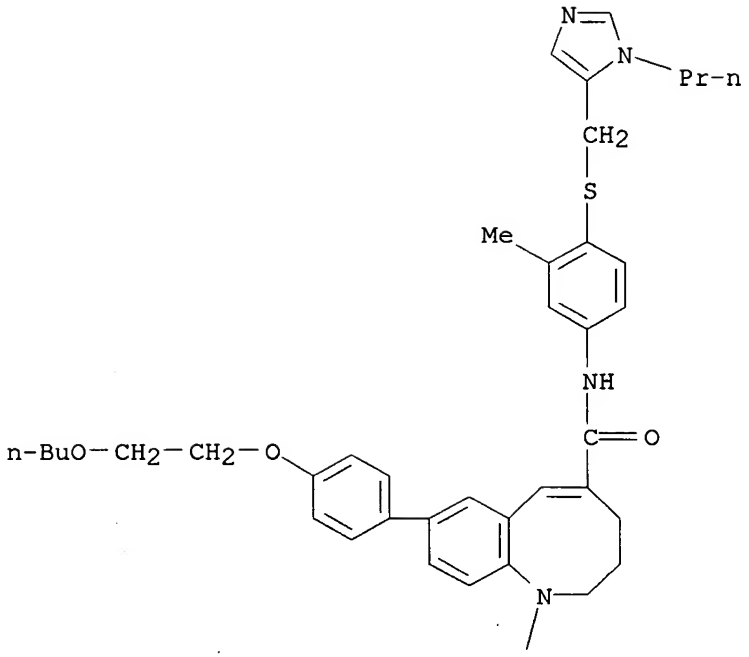
PAGE 1-A



PAGE 2-A

RN 497223-67-3 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[3-methyl-4-[[(1-propyl-1H-imidazol-5-yl)methyl]thio]phenyl]- (9CI) (CA INDEX NAME)

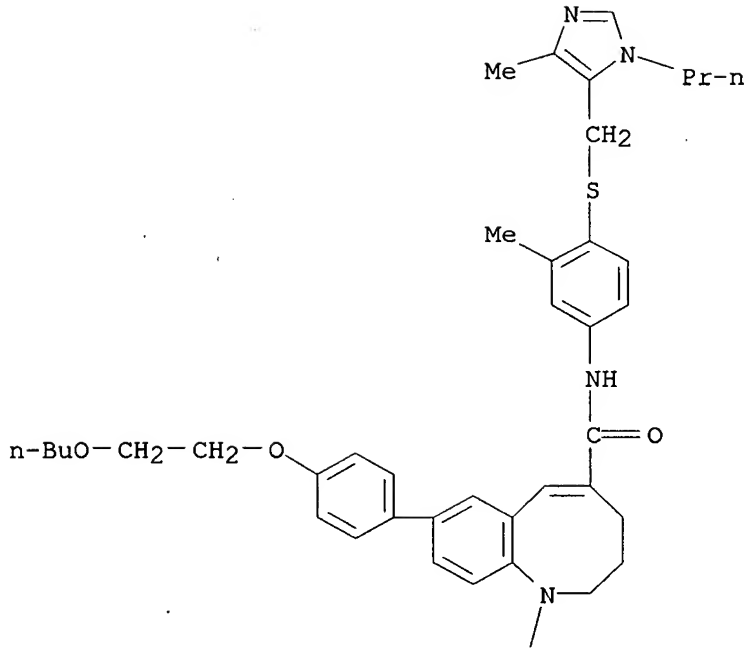
PAGE 1-A



PAGE 2-A

RN 497223-70-8 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-N-[3-methyl-4-[[(4-methyl-1-propyl-1H-imidazol-5-yl)methyl]thio]phenyl]-1-(2-methylpropyl)- (9CI) (CA INDEX NAME)

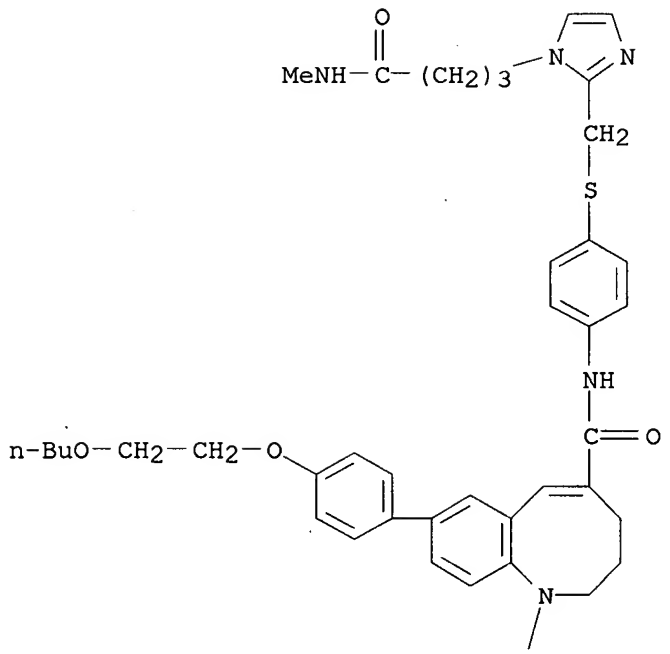
PAGE 1-A



PAGE 2-A

RN 497223-90-2 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-N-[4-[[[1-[4-(methylamino)-4-oxobutyl]-1H-imidazol-2-yl]methyl]thio]phenyl]-1-(2-methylpropyl)- (9CI) (CA INDEX NAME)

PAGE 1-A



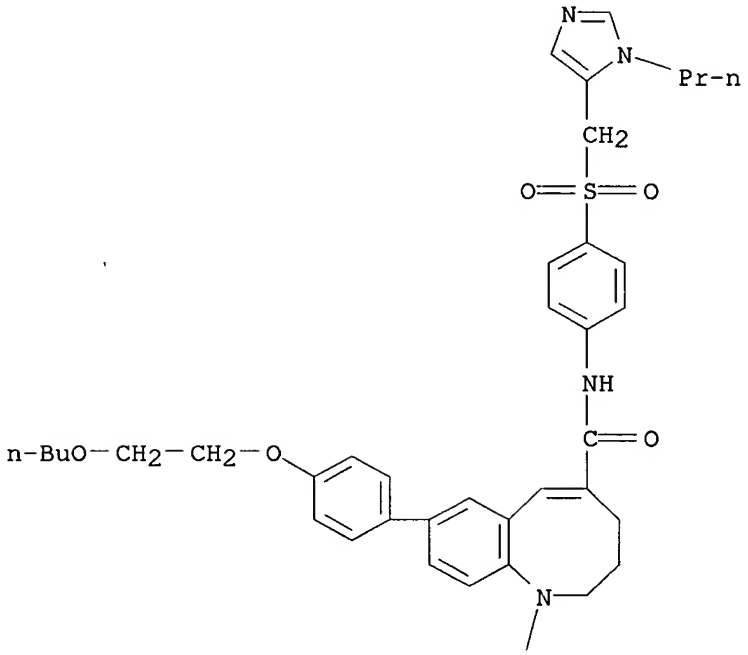
PAGE 2-A

IT 497223-18-4P, 8-[4-(2-Butoxyethoxy)phenyl]-1-propyl-N-[4-[[(1-propylimidazol-5-yl)methyl]sulfonyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-22-0P, 8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfonyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-27-5P, (-)-8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide oxalate 497223-28-6P, (S)-(-)-8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide methanesulfonate 497223-36-6P, (+)-8-[4-(2-Butoxyethoxy)phenyl]-1-propyl-N-[4-[[(1-propylimidazol-2-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-37-7P, (-)-8-[4-(2-Butoxyethoxy)phenyl]-1-propyl-N-[4-[[(1-propylimidazol-2-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-41-3P, (-)-8-[4-(2-Butoxyethoxy)phenyl]-1-(2-methyl-2-propen-1-yl)-N-[4-[[(1-propylimidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-43-5P, (-)-8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-9-methyl-N-[4-[[(1-propylimidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-60-6P 497223-62-8P, 8-[4-(2-Butoxyethoxy)phenyl]-1-phenyl-N-[4-[[(1-propylimidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide

497223-65-1P, 8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[(4-methyl-1-propylimidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-68-4P, 8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-N-[3-methyl-4-[[(1-propylimidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-71-9P, 8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-N-[3-methyl-4-[[(4-methyl-1-propylimidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-74-2P, (S)-(-)-1-Isobutyl-8-[4-(2-propoxyethoxy)phenyl]-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-76-4P, (S)-(-)-8-[4-(2-Propoxyethoxy)phenyl]-1-propyl-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-77-5P, (S)-(-)-8-[4-(2-Propoxyethoxy)phenyl]-1-propyl-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide methanesulfonate 497223-89-9P, Ethyl 4-[2-[[[4-[[[8-[4-(2-butoxyethoxy)phenyl]-1-isobutyl-1,2,3,4-tetrahydro-1-benzazocine-5-yl]carbonyl]amino]phenyl]sulfinyl]methyl]imidazol-1-yl]butanoate 497223-91-3P, (-)-8-[4-(2-Butoxyethoxy)phenyl]-1-(cyclopropylmethyl)-N-[4-[[(1-propylimidazol-5-yl)methyl]sulfinyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide 497223-92-4P 497223-93-5P 497250-40-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of benzazocinecarboxamides and related bicyclic compds. as CCR-5 antagonists for use against HIV infectious and other diseases)

RN 497223-18-4 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-propyl-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfonyl]phenyl]- (9CI) (CA INDEX NAME)

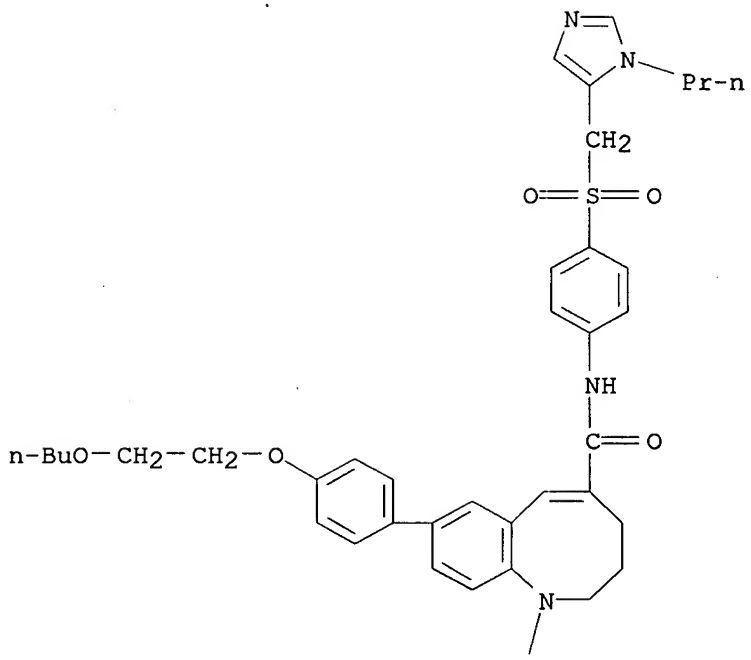
PAGE 1-A



PAGE 2-A

RN 497223-22-0 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfonyl]phenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

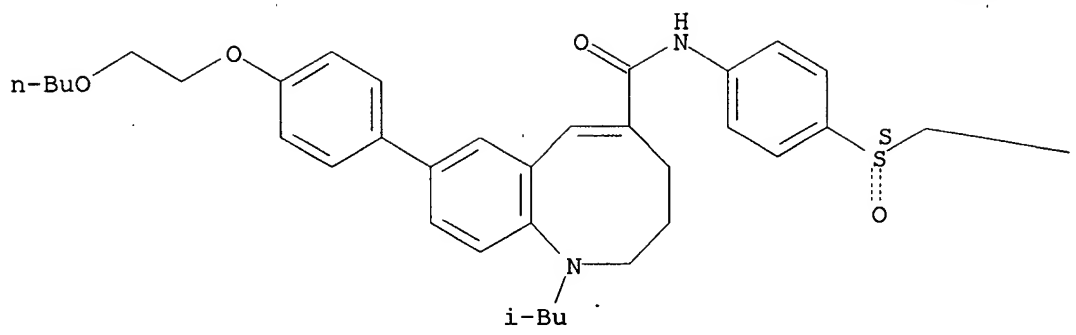
RN 497223-27-5 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

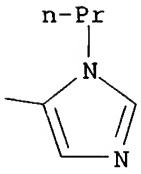
CRN 497223-25-3
CMF C41 H52 N4 O4 S

Absolute stereochemistry. Rotation (-).

PAGE 1-A

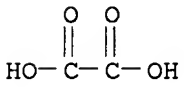


PAGE 1-B



CM 2

CRN 144-62-7
CMF C2 H2 O4



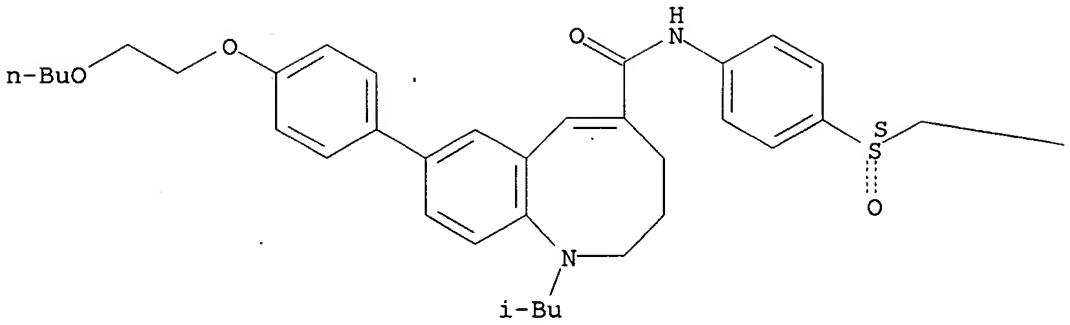
RN 497223-28-6 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

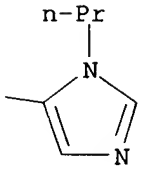
CRN 497223-25-3
CMF C41 H52 N4 O4 S

Absolute stereochemistry. Rotation (-).

PAGE 1-A

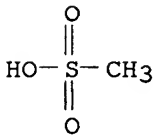


PAGE 1-B



CM 2

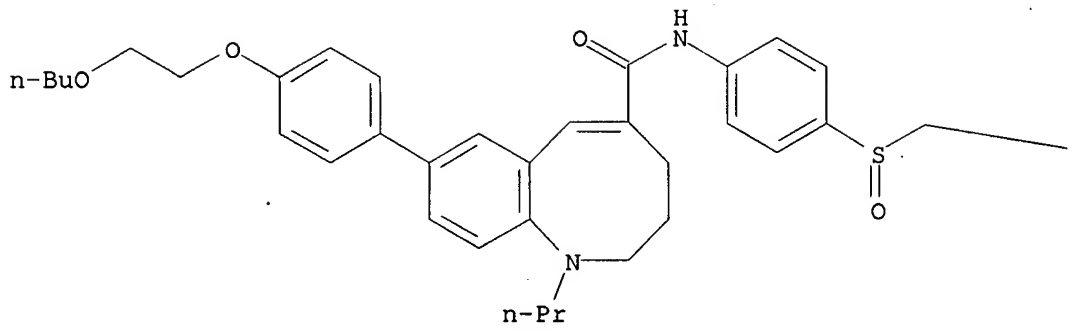
CRN 75-75-2
CMF C H4 O3 S



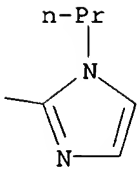
RN 497223-36-6 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-propyl-N-[4-[[(1-propyl-1H-imidazol-2-yl)methyl]sulfinyl]phenyl]-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

PAGE 1-A



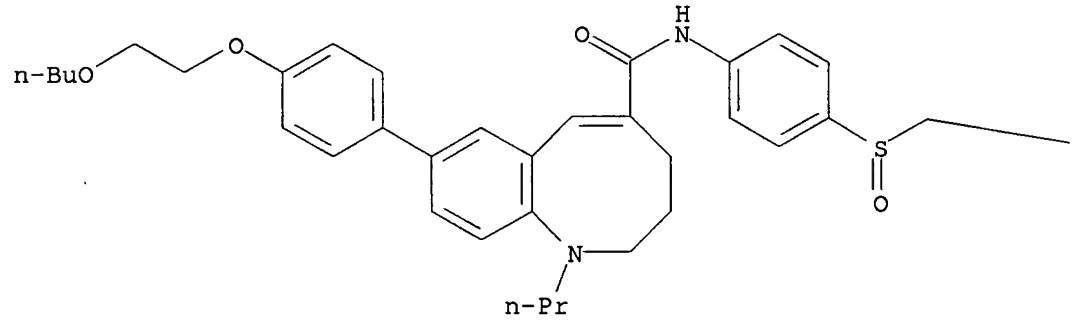
PAGE 1-B



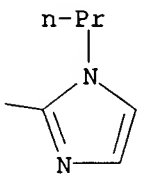
RN 497223-37-7 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-propyl-N-[4-[[(1-propyl-1H-imidazol-2-yl)methyl]sulfinyl]phenyl]-, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

PAGE 1-A



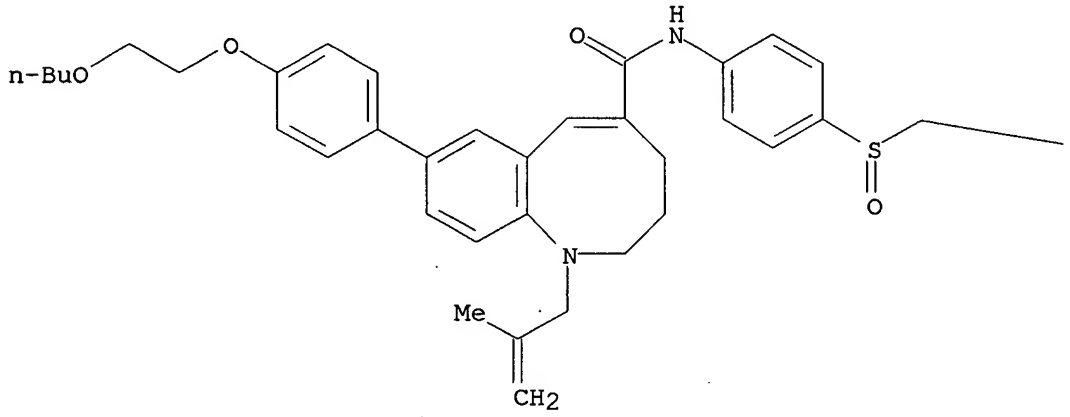
PAGE 1-B



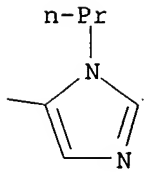
RN 497223-41-3 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methyl-2-propenyl)-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

PAGE 1-A



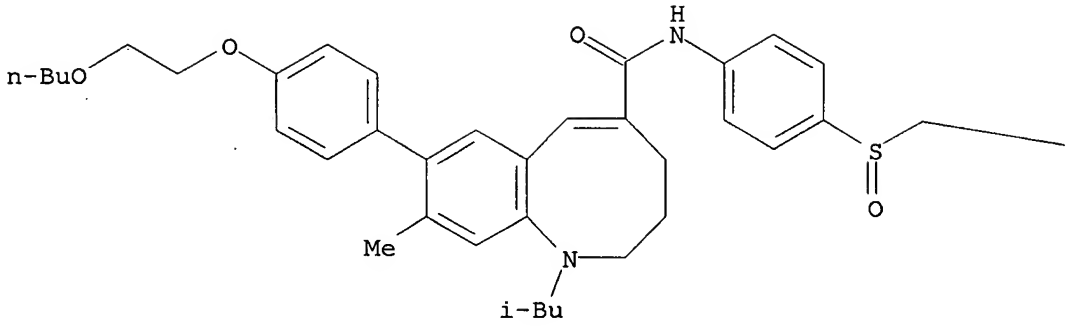
PAGE 1-B



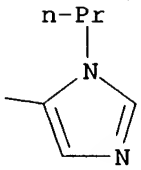
RN 497223-43-5 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-9-methyl-1-(2-methylpropyl)-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

PAGE 1-A



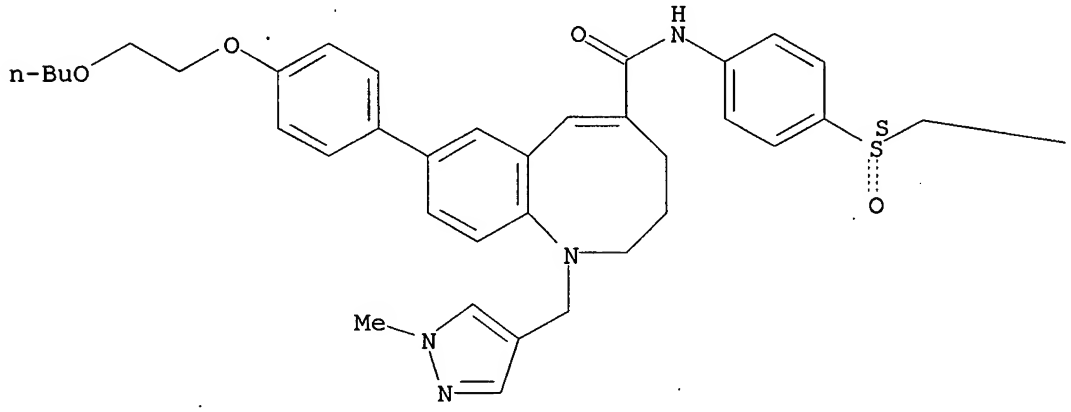
PAGE 1-B



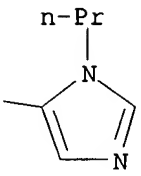
RN 497223-60-6 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-[(1-methyl-1H-pyrazol-4-yl)methyl]-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A

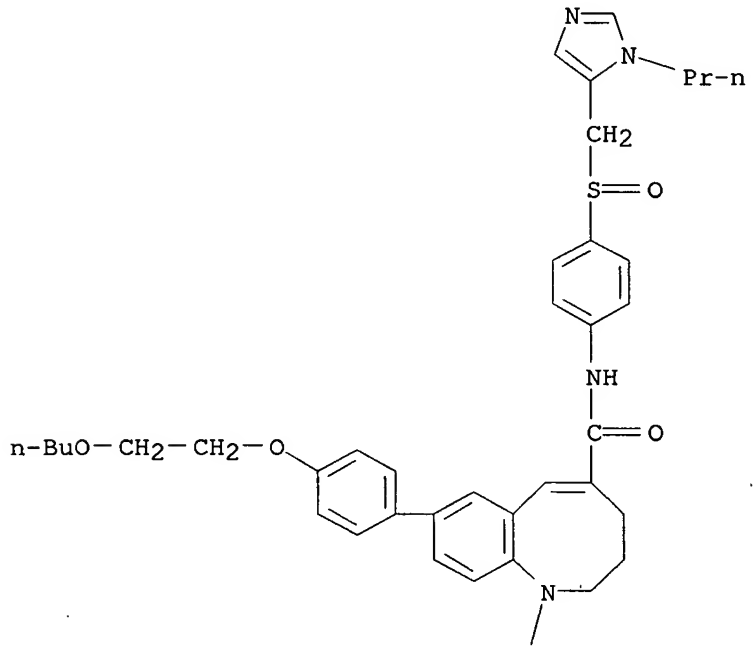


PAGE 1-B



RN 497223-62-8 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-phenyl-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

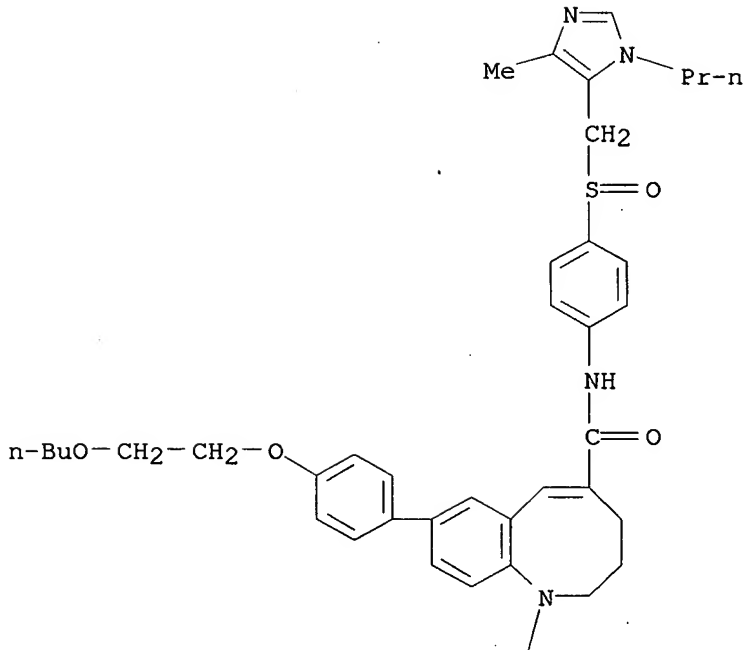
PAGE 1-A



PAGE 2-A

RN 497223-65-1 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[[(4-methyl-1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

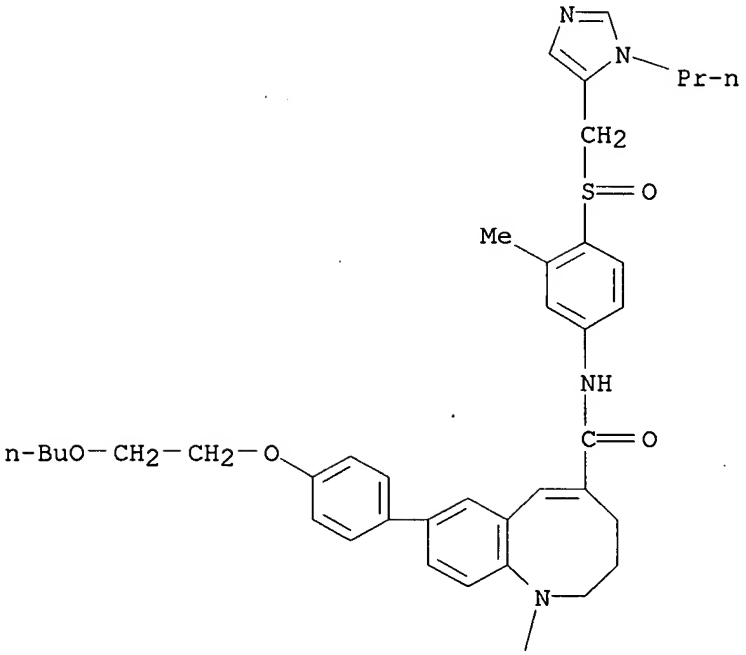
PAGE 1-A



PAGE 2-A

RN 497223-68-4 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[3-methyl-4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

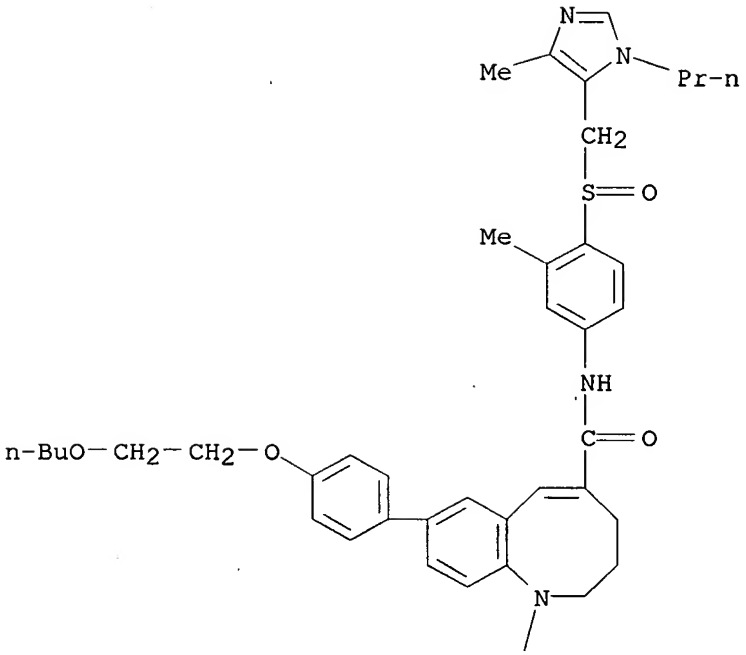
PAGE 1-A



PAGE 2-A

RN 497223-71-9 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-N-[3-methyl-4-[[(4-methyl-1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-1-(2-methylpropyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

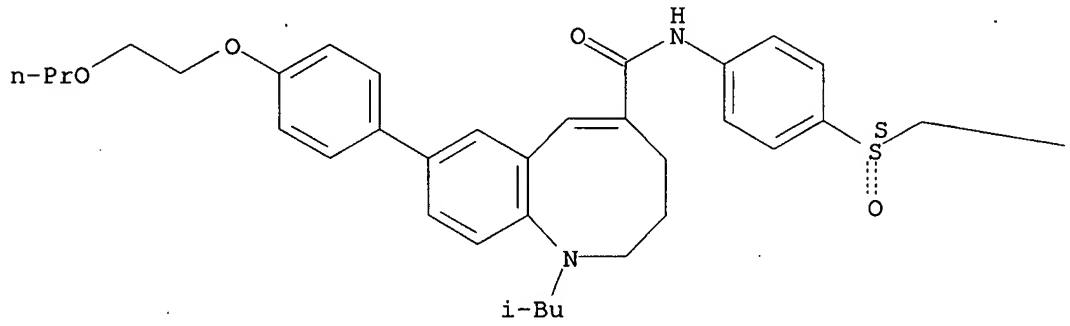


PAGE 2-A

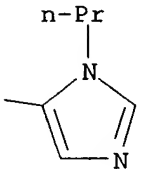
RN 497223-74-2 CAPLUS
CN 1-Benzazocine-5-carboxamide, 1,2,3,4-tetrahydro-1-(2-methylpropyl)-8-[4-(2-propoxyethoxy)phenyl]-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



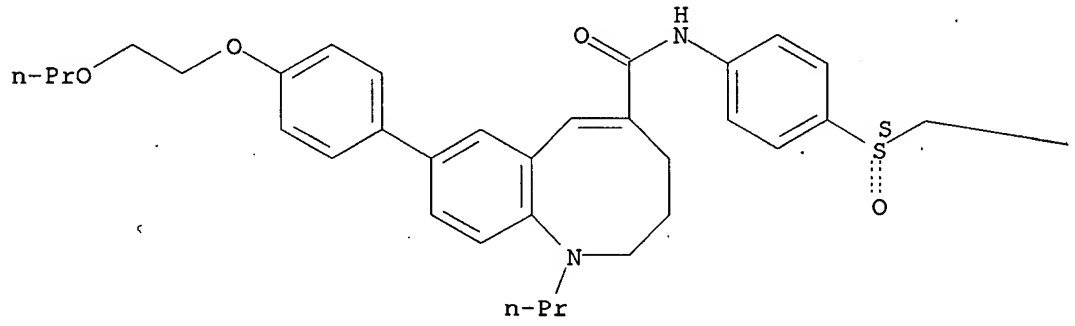
PAGE 1-B



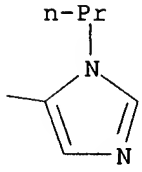
RN 497223-76-4 CAPLUS
CN 1-Benzazocine-5-carboxamide, 1,2,3,4-tetrahydro-8-[4-(2-propoxyethoxy)phenyl]-1-propyl-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 1-B



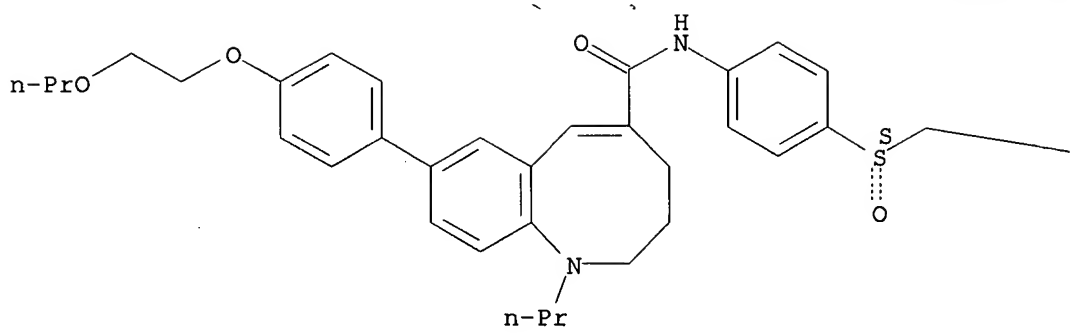
RN 497223-77-5 CAPLUS
CN 1-Benzazocine-5-carboxamide, 1,2,3,4-tetrahydro-8-[4-(2-propoxyethoxy)phenyl]-1-propyl-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

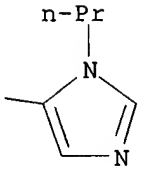
CRN 497223-76-4
CMF C39 H48 N4 O4 S

Absolute stereochemistry. Rotation (-).

PAGE 1-A

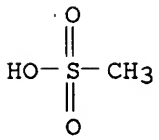


PAGE 1-B



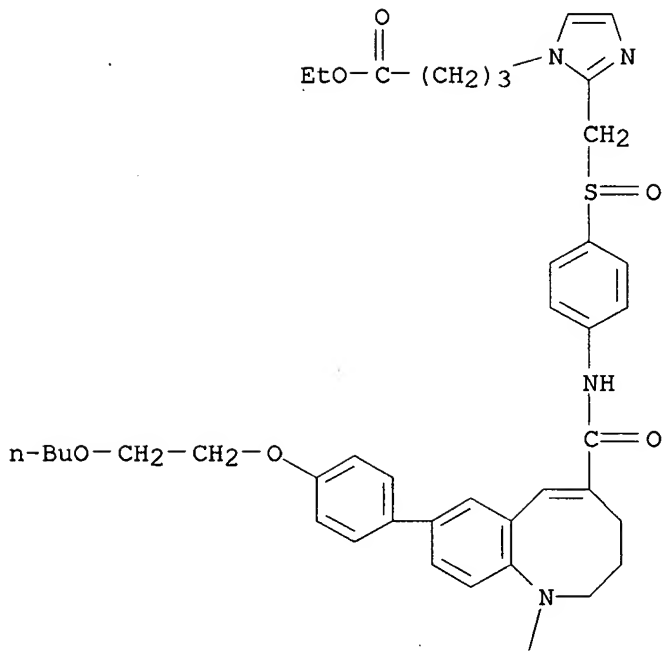
CM 2

CRN 75-75-2
CMF C H4 O3 S



RN 497223-89-9 CAPLUS
CN 1H-Imidazole-1-butanoic acid, 2-[[[4-[[[8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-1-benzazocin-5-yl]carbonyl]amino]phenyl]sulfinyl]methyl]-, ethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

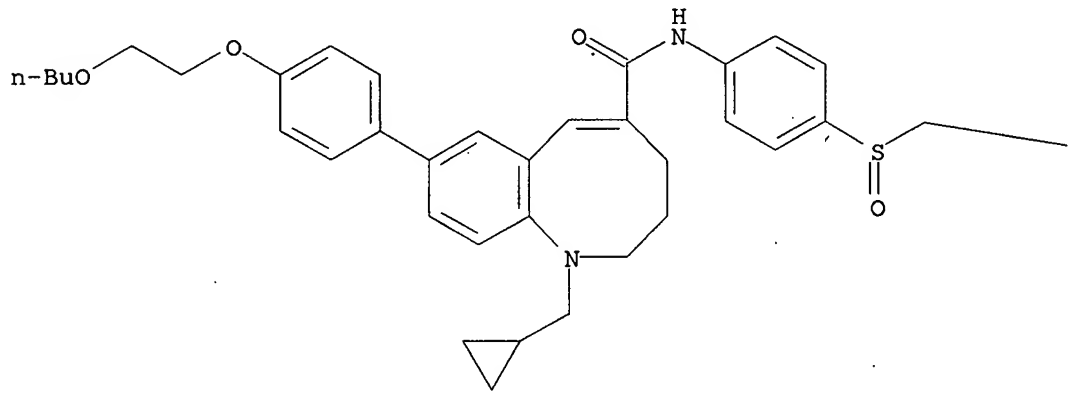


PAGE 2-A

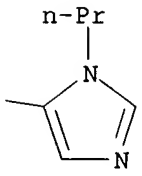
RN 497223-91-3 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1-(cyclopropylmethyl)-1,2,3,4-tetrahydro-N-[4-[[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

PAGE 1-A



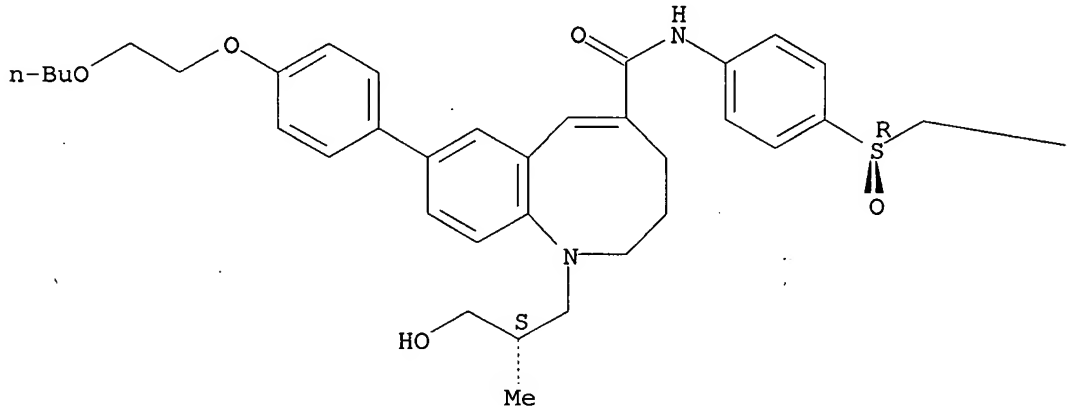
PAGE 1-B



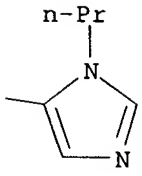
RN 497223-92-4 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-[(2R)-3-hydroxy-2-methylpropyl]-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



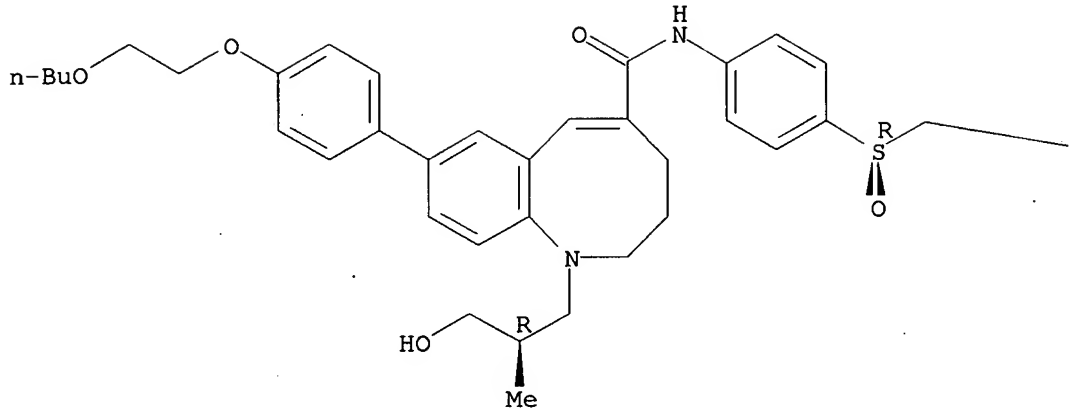
PAGE 1-B



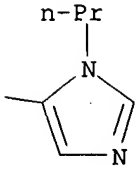
RN 497223-93-5 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-[(2R)-3-hydroxy-2-methylpropyl]-N-[4-[(R)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

PAGE 1-A



PAGE 1-B



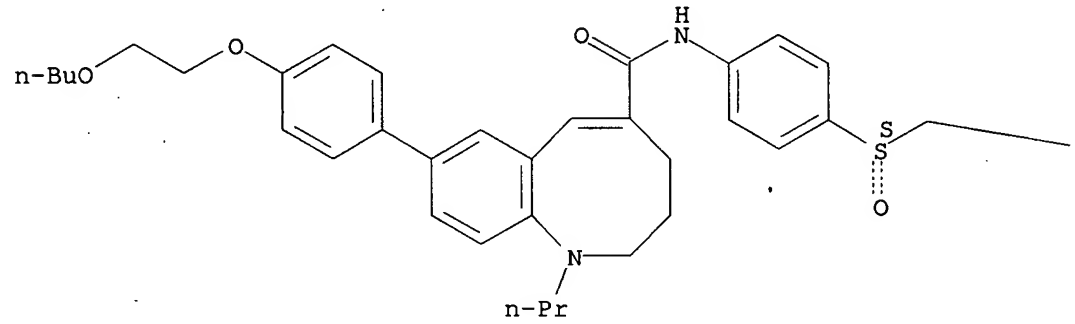
RN 497250-40-5 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-propyl-N-[4-[(S)-[(1-propyl-1H-imidazol-5-yl)methyl]sulfinyl]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

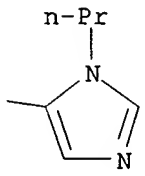
CM 1

CRN 497250-39-2
CMF C40 H50 N4 O4 S

Absolute stereochemistry. Rotation (-).

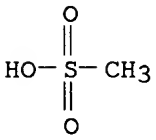
PAGE 1-A





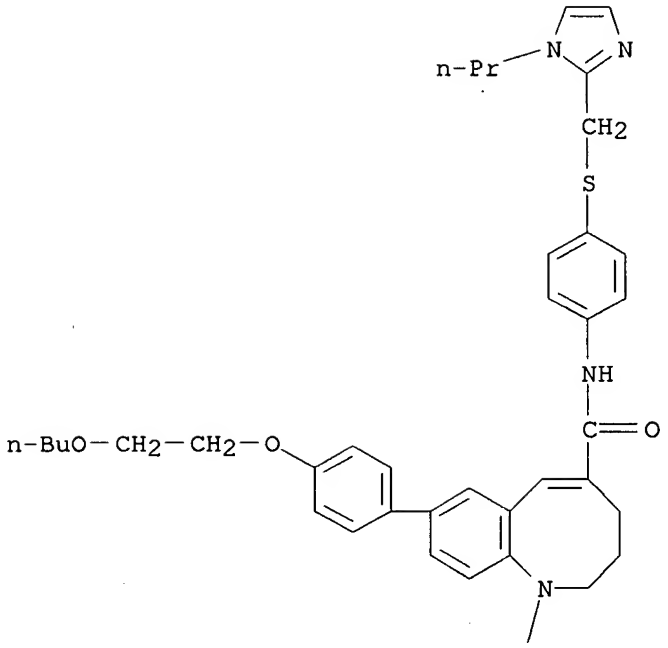
CM 2

CRN 75-75-2
CMF C H4 O3 S



IT 497223-30-0, 8-[4-(2-Butoxyethoxy)phenyl]-1-isobutyl-N-[4-[[(1-propylimidazol-2-yl)methyl]sulfanyl]phenyl]-1,2,3,4-tetrahydro-1-benzazocine-5-carboxamide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of benzazocinecarboxamides and related bicyclic compds. as CCR-5 antagonists for use against HIV infectious and other diseases)
RN 497223-30-0 CAPLUS
CN 1-Benzazocine-5-carboxamide, 8-[4-(2-butoxyethoxy)phenyl]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-N-[4-[[(1-propyl-1H-imidazol-2-yl)methyl]thio]phenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT